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CESAREAN SECTION IN MASSACHUSETTS IN 1940*

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THIS report is the fourth of the five-year study of cesarean sections sponsored by the Massachusetts Department of Public Health and the Section of Obstetrics and Gynecology of the Massachusetts Medical Society.

Questionnaires were sent to one hundred and seventy-two licensed maternity hospitals, and replies were received from all except one small proprietary hospital. The care given the preparation of the replies varied greatly. The co-operation of those hospitals that replied carefully and intelligently to the questionnaires is appreciated. In thirty-nine hospitals, no cesarean sections were performed.

* * *

In Massachusetts in 1940, there were 66,496 live births and 1765 stillbirths, a total of 68,261. Of these, 56,935 were reported to us as having occurred in hospitals. Two thousand three hundred and twelve cesarean sections are recorded. One emergency section was done in a home. There were 21 hysterotomies, making a total of 2333 abdominal deliveries.

The incidence in 1937 was 1:30.3, in 1938, 1:28.7, in 1939, 1:32.2, and in 1940, 1:29.2.

Table 1 gives a summary of the abdominal deliveries. There was a greater proportion of elective sections than before, and a little larger percentage of low sections.

There were 26 of the extraperitoneal type, 16 being of the Waters type. All but 2 of the patients in this group lived. Twenty-two babies lived, but 5 were stillborn. The deaths are discussed below. It should be remarked that the convalescences in this group were greatly improved over those occurring in 1939. In 1 case of the peritoneal-exclusion type, the patient had a stormy convalescence because of sepsis, but eventually recovered. Two others developed sepsis, with stormy convalescence, and made slow but final recovery. One patient was infected with gas bacillus but eventually recovered.

There were 34 Porro operations, or hysterectomy following immediately or shortly after the cesarean section. The indications for these 34 cases are varied. Eight were done for uncontrollable hemorrhage. One of these patients, a case of placenta previa, when operated on, was found to have a placenta accreta. Seven operations were done for fibroids of the uterus. In 5 cases, the only reason given was that the patient had had a previous section, but in only 1 of these had two sections been done. In 5 cases, a ruptured uterus was found. The following indications each accounted for 1 case: eclampsia, toxemia, pyelonephritis, age of patient (forty-four), a long labor and patient infected, and a shoulder presentation with a contraction ring. In 1 case, I have classified the indication as bizarre, — "necessity for pelvic operation." In 1 case, there was no recorded indication, and in the final case, the indication given in the questionnaire was "attempted breech extraction, with inability to deliver the head." That indication suggested very bad obstetric judgment, and on fur-

TABLE 1. *Summary of Abdominal Deliveries.*

OPERATION		NO. OF CASES
Cesarean section		2312
Emergency	1051	
Elective	1247	
Not reported	14	
Type of operation:		
Low	1235	
Classical	992	
Latzko, Waters or extraperitoneal	26	
Porro	34	
Not reported	25	
In labor	757	
Not in labor	1491	
Not reported	64	
Membranes ruptured	368	
Membranes unruptured	1884	
Not reported	60	
Hysterotomy		21
Total		2333

*Presented, in part, before the Boston Obstetrical Society, January 20, 1942.

ther inquiry it was learned that the patient was in labor a long time and that x-ray examination showed a breech presentation with a definite hydrocephalic head. Since the fetal heart was heard, the operator did a section and then a Porro. In this group, 14 babies died, and 21 survived. Five of the mothers died, but these are reported under the maternal deaths.

Table 2 records the indications for the hysterotomies, and needs no comment.

Table 3 shows the various types of anesthesia used. The only change noted is the great increase in the use of spinal anesthesia. It should be mentioned that in 1 case the patient was prepared for a section, was given a spinal anesthesia and died as the abdominal incision was made. The case cannot be classified as a death from cesarean section, but it is recorded among the maternal deaths occurring in Massachusetts in 1940. In the group classified as "other," there were various combinations of basic drugs with either cyclopropane, ether or nitrous oxide.

TABLE 2. *Indications for Hysterotomy.*

INDICATION	NO. OF CASES
Cardiac disease	5
Hypertension	5
Pyelonephritis	3
Tuberculosis	2
Separated symphysis	2
Manic-depressive insanity	2
Chronic nephritis	1
Progressive muscular atrophy	1
Total	21

TABLE 3. *Types of Anesthesia.*

ANESTHETIC	NO. OF CASES
Nitrous oxide, oxygen and ether	1355
Ether	261
Cyclopropane	144
Spinal	396
Nitrous oxide and oxygen	5
Avertin, and nitrous oxide, oxygen and ether	27
Local	32
Other	70
Not reported	22
Total	2312

Table 4 presents the indications for operation in cases in which the baby was lost. As one might expect, emergency operations accounted for the large majority of these infant deaths. In the elective-section column, several can at once be excluded from criticism. In 2, the babies were macerated. Two mothers had diabetes. One had chronic nephritis, and the section was done in the interests of the mother. Three babies had malformations incompatible with life — meningocele, diaphragmatic hernia and congenital abnormality of the bile ducts. Five deaths in the elective column were assigned to monstrosities; all the fetuses were hydrocephalic. Not all these cases had x-ray study before operation. Subtracting these 13 cases, there were still 52 elective sections in which the baby was lost. It is unnecessary to review these deaths. It is sufficient to call attention to the fact that serious criticism is justified when a baby is lost following an elective section. Either the time chosen or the technic is at fault, and the operators should rightly be reprimanded.

In the emergency column, as has been remarked in previous reports, it is doubtful if sections should have been done for the first two indications — separated placenta and placenta previa.

TABLE 4. *Indications for Operation in Cases with Death of the Baby.*

INDICATION	EMERGENCY CESAREAN SECTION	ELECTIVE CESAREAN SECTION
Separated placenta	49	0
Placenta previa	49	7
Toxemia	4	10
Eclampsia	3	0
Previous cesarean section	18	22
Inefficient labor	4	0
Disproportion	1	4
Contracted pelvis	3	5
Dystocia	2	0
Ruptured uterus	4	0
Previous operative attempts	2	0
Test of labor	4	0
Cardiac disease	1	2
Malposition	6	0
Monstrosity	6	5
Elderly primipara	1	0
Breech presentation	3	0
Previous surgery	1	3
Medical indications	0	4
Cervical dystocia	2	0
Previous disaster	0	1
Young primipara	0	1
Fetal distress	1	0
Uterine inertia	1	0
Prolapsed cord	1	0
Bicornate uterus	1	0
Bizarre	1	1
Not reported	1	0
Totals	169	65

To go over each indication would make a tiresome review, but certain points should be noted. Under "monstrosity," there were 6 cases of hydrocephalus. The majority were not so diagnosed before operation. Malposition of the heart, congenital atresia of the esophagus, and diaphragmatic or ventral hernia cannot be diagnosed before operation, but major skeletal deformities should be, if careful x-ray films are taken.

The chief reason for the loss of the babies under the indication, "previous section," was prematurity. Either labor had begun or the membranes had ruptured before term. Many of these patients were operated on after they were in labor.

It is obvious that the number of babies lost is too large. The operators should weigh the probability of obtaining a living baby more carefully than they obviously did. It is surely questionable obstetrics to do an emergency section because a fetus shows distress, and then obtain a hydro-

cephalic baby. This is true of other indications. Until the infant mortality is reduced, the results in cesarean section cannot be regarded as satisfactory.

Table 5 shows the indications given for operation. It is to be expected that the operations for "previous section" will increase steadily because of the great number of new sections done each year.

I shall not discuss each indication, but there are certain comments that I wish to make. Many of the sections for placenta previa were done at five, six or seven months' gestation, with no probability that the babies would live. The same thing is true of the indication, "separated placenta."

The number of cases done because of eclampsia in 1940 was larger than that in any previous year — 15. Of course, when eclampsia occurs, somebody has erred, either the patient or the physician. But to subject a woman already desperately sick from eclampsia to a section is regarded by the majority of obstetricians as a doubtful procedure. In 1940, 3 eclamptic mothers died.

Under the indication, "malposition of the baby," an increasing number of sections are done for breech. A section on a primiparous breech may be justifiable in many cases. But to operate because of a multiparous breech is not good obstetrics. Whether many of the transverse presentations could have had external versions or simple internal podalic versions at an elected time is a difficult question to settle, but there has been a great increase in the number of sections for this indication.

Under "dystocia," an attempt has obviously been made to use the test of labor in a greater number of cases. But the test of labor is a very indefinite thing, varying from one or two hours to twenty-four or forty-eight hours, with or without rupture of the membranes. In many of the cases of "labor without progress," it was definitely stated that the patient had had only an occasional pain. In some cases of "cervical dystocia," the patient was not even in labor, and yet a section was done for that indication.

It is doubtful if everyone would agree on the indications classified under "previous surgical operations." Undoubtedly, many of these were justifiable, and to state dogmatically that they were not would be unfair. I have continually questioned the advisability of doing sections on so many patients who have had a repair of the perineum. From the questionnaire, there is no way of evalu-

TABLE 5. *Indications for Cesarean Section.*

INDICATION		NO. OF CASES
Previous section		726
Contracted pelvis and disproportion		350
Contracted pelvis	204	
Disproportion	146	
Placenta previa		211
Separated placenta		109
Toxemia		107
Eclampsia		15
Malposition of baby		113
Breech	73	
Transverse	20	
Brow	4	
Face	6	
Compound	1	
Shoulder	2	
Right occipitoposterior	4	
Chin posterior	1	
Left parietal	1	
Type not noted	1	
Dystocia		279
Dystocia	32	
Labor without progress	51	
Test of labor	127	
Cervical dystocia	44	
Contraction ring	3	
Uterine inertia	22	
Previous surgical operations		56
Repair of perineum	21	
Amputation of cervix	16	
Myomectomy	5	
Pelvic surgery	3	
Uterine surgery	3	
Fracture of both bones, lower leg	1	
Congenital hip	1	
Previous abdominal operation	1	
Perineal abscess	1	
Acute appendicitis	1	
Strangulated umbilical hernia	1	
Previous nephrectomy	1	
Previous operation on spine	1	

INDICATION		NO. OF CASES
Associated medical conditions		51
Cardiac disease	27	
Tuberculosis	3	
Diabetes	13	
Carcinoma of cervix	1	
Purpura hemorrhagica	1	
Myasthenia gravis	1	
Fibrosis cystica	1	
Acute back	1	
Chronic nephritis	1	
Paroxysmal tachycardia	1	
Schizophrenia	1	
Early rupture of membranes		2
Previous obstetric disaster		73
Elderly primipara		57
Young primipara		1
Obstructing tumors (fibroids)		21
Fetal distress		7
Prolapsed cord		4
Previous operative attempts		8
By request or for sterilization		9
Request	4	
Sterilization	5	
Ruptured uterus		4
Spontaneous	2	
Previous section	2	
Bicornate uterus		1
Postmaturity		8
Malformation of fetus		9
Malformation of vagina		2
Twins		3
Floating head		3
Varicosities		1
Bizarre		19
Not reported		63
Total		2312

ating the indications, "pelvic and uterine surgery." Surely "fracture of both bones, lower leg" is specious. I cannot understand the indications, "perineal abscess" and "acute appendicitis." If the latter was a definite acute appendix, surely to follow it by a section was a very dangerous procedure. In this case, to quote the operator, "it was explained to the husband that a cesarean section was advisable since there would be a great danger of evisceration of the abdominal wound during normal labor, which was due in ten days."

The indications listed under "associated medical conditions" need little comment. It must be remembered that a section in a severe cardiac condition is a serious procedure and not always the best way to deal with the condition. Each year, deaths are recorded in this group, and in 1940 there were 3.

In previous reports, the reason for the increasing number of sections on diabetic patients has been mentioned. In 1940, there were 13 new sections for this condition, and 5 others were classified under "repeat sections." No mothers were lost, but 3 babies died, 1 was macerated, and 1 had a cystic kidney.

A somewhat astonishing indication is "acute back."

Following "associated medical conditions" in this table, one finds a miscellaneous list of indications. Some of these are valid, but others are not.

"Previous obstetric disaster" is in many cases a reasonable indication. But the circumstances surrounding the previous delivery must be thoroughly studied — the type of labor, the size of the baby and, above all, the ability of the physician in charge of that disaster.

In many elderly primigravidas, a section is surely justified, but the mere fact that the patient is older than many women having their first babies is no good indication. The size of the baby, its relation to the pelvis and the condition of the cervix are determining factors. If the decision is to operate, an elective section should give the best results. This year, 2 mothers in this group were lost following emergency sections.

There seems to be no justification for doing a section simply because the patient is young (fourteen), unless there is some definite indication.

The advisability of operating because of fetal distress has been consistently questioned. More justifiable, if conditions are good, is operation for a prolapsed cord when the cervix is not fully dilated.

Regarding the indication, "following operative attempts," it should be repeated that at best this is a dangerous procedure. Of the 8 cases so classified, 4 followed the unsuccessful application of forceps. Three of these patients had stormy convalescences. One, on whom a Waters section was done, made a good recovery. One baby was lost. Three patients had malformed babies, 1 being a double-headed monstrosity. In this case, the questionnaire states: "Forceps tried and failed, then decapitation and attempted forceps on the other head, followed by attempted version and extraction. Finally a cesarean section of the peritoneal exclusion type was done. After a very stormy convalescence, the patient recovered." It is obvious from the questionnaire that this was a most difficult case to manage, and the operator was fortunate that the patient did not die.

Two fetuses were hydrocephalic. It is stated in one case that a craniotomy was done, but since the head did not engage, a low section was performed. The obstetric judgment in not completing the delivery following craniotomy is open to question. In the other case, the note states, "Attempted breech extraction to midthigh; delivery failed, and a section was then done." This case is considered under the maternal deaths.

The next indication, "for sterilization or by request," cannot be considered justifiable.

Four cases are recorded under "ruptured uterus," 2 being spontaneous and 2 following previous sections. These cases were so diagnosed. There were, however, 6 others that were discovered at operation following previous sections.

The indication, "postmaturity," is questionable, especially when the questionnaire says "one week overdue." In 1 case, the patient was stated to be two and one-half weeks overdue, with a large abdomen; a section was done, and twins were delivered. The mother died. The case is commented on below.

With a known malformation of the fetus incompatible with life, cesarean section is not justifiable without other indication.

In 3 cases, the only indication given was "twins." In 1, the pelvis was reported as rachitic. In this case, the babies weighed 6 pounds, 8 ounces, and 6 pounds, 4 ounces. There were 18 other cases of twin pregnancy and 1 case of triplets, but these were all assigned to other indications than "multiple pregnancy."

In 3 cases, the only indication given was "floating head (patient not in labor)." There was no note of the relation of the size of the head to the pelvis, or whether the patient was approximately at full term. That a floating head can be regarded as an adequate indication is doubtful.

The indication, "Varicosities," is also open to criticism, unless the condition is very severe.

The 19 cases classified as "Bizarre" need not be taken up in detail. Several were classified as "dys-

tocia," although the patients were not in labor. In 2 cases, the only indication was "multiparity." One baby weighed 6 pounds, 11 ounces, and the other weighed 7 pounds, 11 ounces. In another case, it was stated that the patient had "soft-tissue dystocia," and yet there was no labor. In another, the only indication was "necessity for pelvic operation." One indication was, "Severe persisting labor for three days; fainting spells, with vomiting; question of concealed hemorrhage." A section was done, and the baby, in good condition, weighed 7 pounds, 9 ounces.

One indication given was:

> The following sociological condition: The patient was living with her husband's family, with no opportunity to go on her own. The family were very critical of her repeated pregnancies, this being her third. Because of this and the facts that she had a third-degree tear with a good repair, that she was very desirous of having her tubes tied off, and that the baby was a large one, a cesarean section was done.

Another indication was a "fixed cervix." What that means, I do not know. There was no labor. The baby was born dead. There was 1 case of "locked twins." In the final case, a classical section was done because "the vagina had been explored at six months." The patient had no labor. The baby weighed 6 pounds, 12 ounces.

There were 63 cases in which no indication was recorded. Doubtless, the indications were good and sufficient, but the questionnaires did not show them.

Table 6 presents a summary of the 41 maternal deaths that occurred in 1940. Deaths from emergency sections are always more frequent than

TABLE 6. *Summary of Cases with Maternal Death.*

DATA	NO. OF CASES
Emergency operation	33
Elective operation	8
Type of operation:	
Low	15
Classical	20
Waters	2
Porro	4
In labor	22
Not in labor	19
Membranes ruptured	17
Membranes unruptured	24
Babies:	
Living	36
Dead	8

those from elective sections. The situation in 1940 is unchanged. The number of deaths following elective sections (8) is the lowest that has been recorded.

The other figures need no comment.

Figure 1 shows the indications and the causes of death in the elective sections. There were 6 repeat sections: 2 patients died from sepsis, 1 from thrombosis of the superior mesenteric artery, 1 from embolus, and 2 from hemorrhage.

In the first of the 2 deaths from hemorrhage, autopsy revealed a most unusual condition. The patient had had five previous sections. At this operation, a low transverse section was done. At the time of operation, it was noted that the previous incisions were covered by large varicosities. The patient was returned to the ward in good condition. Four hours later, she suddenly went into shock. In spite of transfusion and stimulation, she died. At autopsy, the abdominal cavity contained much blood and one clot the size of a grapefruit.

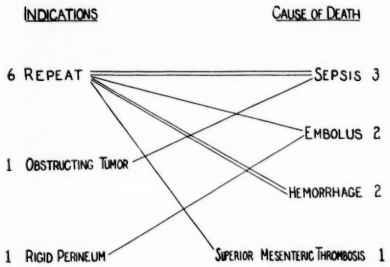

FIGURE 1. *Maternal Deaths in 8 Elective Cesarean Sections.*

The old scar was gaping wide open, but the new scar was intact. There is no note regarding the varicosities.

In the other death from hemorrhage, the cause given on the death certificate was "shock due to cesarean section." On investigation, it was found that because of excessive loss of blood at the operation the patient was in poor condition. The operator, a general surgeon, left immediately after the operation. In the absence of the operator, treatment consisted in the administration of stimulants.

Two cases were assigned to embolus. I wish to comment on 1. In the questionnaire, the indication for the section was "contracted pelvis, rigid perineum and narrow introitus." Convalescence was normal, and at the end of fourteen days, the patient was about to be taken home when she complained of severe exhaustion and weakness. She suddenly expired from an embolus. It was reported by the investigator who looked up this death that the patient had a transverse position with knee and elbow presenting. On the tenth day, she was up and about to go home when she felt faint and weak and was put back to bed and kept there for two weeks longer. She was about to be transferred by ambulance when she suddenly died. This patient probably did die from an embolus,

but the history as given in the questionnaire and the story as obtained by the physician who investigated the death show so great variance both in the indications for operation and in the convalescence that it seems worth noting.

The cause of the final death under elective sections was given as "obstructing tumor." This patient died of sepsis.

Figure 2 shows the indications and the causes of death in the 33 emergency sections.

Ten patients were classified as dying from sepsis. Seven of these were so diagnosed on the death certificate. Of the other 3, one was reported on the questionnaire as dying from bronchopneumonia,

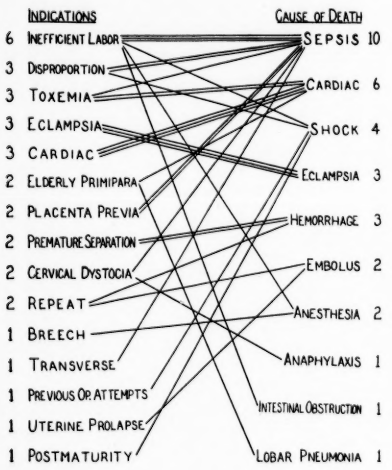

FIGURE 2. *Maternal Deaths in 33 Emergency Cesarean Sections.*

and another from embolus. The third is considered below. Autopsy on the first of these showed multiple abscesses of the uterine wall and multiple pulmonary emboli. The second patient ran a temperature of 100 to 101°F. each day after the operation. At autopsy, a thrombosis of the pelvic veins was found. This patient undoubtedly had an embolus, but she was also septic and was therefore so classified. Possibly, this death should be classified as due to embolus.

The third case deserves comment. The indication for operation as given in the questionnaire is as follows: "The patient was a para III. Examination showed uterine inertia, primary and secondary; uterine anomaly, nonpathologic; cardiorenal disease; pre-partum toxemia; uremic syndrome; and pernicious anemia." The questionnaire states that a classical section was done; the membranes were not ruptured, and the patient was in labor fifty-two hours. The causes of death were given as follows: "pregnancy, uterine inertia, pernicious anemia, post-partum toxemia, intestinal obstruction and circulatory failure."

The investigator's note is as follows:

> The patient ran a postoperative temperature of 103 to 105°F. There was no indication of pernicious anemia by signs, symptoms or laboratory study. A low section was done following a twenty-four-hour labor, with full dilatation for four hours. The doctor who operated stated that the membranes were unruptured but bulged out through the vagina. He saw something in the front part of the vagina that he designated "nonpathologic uterine anomaly." The patient had had two normal deliveries.

This patient obviously died of sepsis. The case was misdiagnosed and mistreated throughout. Death must be laid at the door of the physicians and of the hospital that allows such men to carry on.

The indications for the section in 10 patients who died of sepsis were: inefficient labor, 3; disproportion, 2; toxemia, 1; placenta previa, 2; so-called "cervical dystocia," 1; and transverse presentation, 1. In this group, 5 classical sections were done, 4 being of the low and 1 of the Waters type.

It seems poor judgment to do a classical section on a woman who has been in labor many hours with ruptured membranes. The risk that such an operation entails has been established for many years.

Four deaths are classified as due to shock—1 following inefficient labor, 1 with the patient in labor for twelve hours with disproportion, 1 in which an operative attempt failed and 1 with the questionable indication of "postmaturity."

It is interesting to go a little farther into these cases. In the first, the indication was a long labor with a high presenting part and no dilatation of the cervix. The length of labor was not stated. But the physician who investigated the case found that the patient was in labor sixteen hours without progress, that she died four hours after operation and that she was transfused three times.

The second patient died three hours after operation. On the questionnaire, there was no further comment, but it was discovered by the investigator that she had received 21 gr. of Seconal within twelve hours, and it was believed that this large amount of Seconal had something to do with the death.

The case in which operative attempt failed needs explanation. The indication given on the questionnaire was, "On attempted breech extraction to

the midthigh, it was impossible to deliver the child; therefore, a section was done." The patient died of shock an hour after leaving the operating room, and the baby was stillborn. On investigation, the following facts were elicited. The patient had eight living children. The present baby was not of excessive size. The patient had a twenty-four-hour labor, with ruptured membranes. Many vaginal examinations were made. Delivery by forceps was attempted three times, followed by an attempted version and extraction. All this was done previous to a classical section.

In the case in which the indication was given as "postmaturity," it was stated that the patient had a very large uterus and that she was two and one-half weeks overdue. The physician tried to induce labor with quinine and castor oil, without effect. The patient was in labor twelve to fourteen hours, when a section was done and twins were delivered, one weighing 5 pounds, 13 ounces, and the other, 5 pounds, 8 ounces. The operation was done by a general surgeon, and there is no record that an x-ray examination was made. There seems no real indication for this section. The patient failed very quickly after leaving the operating room and died soon afterward. The twins left the hospital in good condition.

Six deaths are classified as due to cardiac conditions. Two of these patients were known to have bad cardiac conditions during pregnancy. Another was found moribund, supposedly because of a bad heart condition, having had no medical care whatsoever, and the physician did an emergency section in the home without previous preparation, with the hope of obtaining a live baby. The baby was stillborn.

In still another case, the patient was a forty-four-year-old primipara, who apparently had acute cardiac decompensation with pulmonary edema shortly after operation.

Two sections were done because of toxemia, one very severe and the other mild. The latter patient had triplets. She went to pieces shortly after the operation and died in spite of all stimulation. The three babies lived. The other patient was a Christian Scientist who had had no satisfactory medical care. She developed a congestive heart failure while in labor and was digitalized; a section was done under local anesthesia. The baby died.

There is nothing to be said of the 3 eclamptic deaths, except that a section is not at present regarded as good treatment in such cases. The 3 babies survived.

In the 3 cases of hemorrhage, 2 sections were done for separated placenta. In the first of these, the patient had been bleeding off and on during the entire pregnancy. She was hospitalized at the seventh month and kept in bed for three weeks until it was thought that the baby was viable. At operation, she bled very profusely, and continued to bleed after the section was completed. She was transfused during the section and five times thereafter. An hour after operation, a hysterectomy was done. The baby did not survive. In the other case of separated placenta, the patient oozed from the arm where blood had been taken, and at the operation the uterus failed to contract satisfactorily. Four hours after operation, a hysterectomy was done while she was in very bad shape, and she died half an hour later. She was given a total of 3000 cc. of blood. These 2 cases show the necessity, when the uterus fails to contract, of doing a hysterectomy at once instead of delaying until the patient is in a desperate condition.

The third death was due to placenta previa and placenta accreta. This patient had been in bed at home for three weeks with a small amount of staining of pinkish fluid. She suddenly had a tremendous hemorrhage, and a section was done. As soon as the accreta was diagnosed, a supravaginal hysterectomy followed, but the bleeding continued. The patient died on the table. The baby did not survive.

I have classified 2 deaths as caused by embolus. One followed a repeat section. Following the operation, which was of the extraperitoneal type, the patient ran a fever. She was thought to be in satisfactory condition to go home when she suddenly had an embolus and died. Autopsy showed that there was a small amount of pus at the lower end of the abdominal wound and a thrombosis of the right iliac vein. This patient in all probability had a low-grade sepsis.

The other case of embolus needs a little elaboration, for the questionnaire and the report given on investigation of the death are at variance. The questionnaire states that the indication was toxemia of pregnancy due to a nephritic condition, with vaginal bleeding. A classical section was done. An uneventful recovery from anesthesia followed. On the sixth day, the patient had an embolus and died. On investigation, the following facts were discovered. The patient had had two previous normal pregnancies. During this pregnancy, she had had slight irregular spotting. There was no bleeding on entrance or before the operation. The patient was hospitalized at the seventh month, and the hospital record states that there was an existing uterine prolapse. The surgeons in this hospital elected to operate and did a Porro section at seven months. The patient did die from an embolus, but the necessity for the operation is more than questionable.

Two cases are classified as due to "anesthesia."

In one, the indication was a breech, and in the other, inefficient labor. In both cases, the cause of death was given on the questionnaire as pulmonary embolus, but in each case the patient was cyanotic throughout the anesthetic, with a large amount of mucus and frequent vomiting. There is no doubt that both patients had pulmonary edema, and possibly acute dilatation of the heart, but the underlying cause of death was a poorly given anesthetic.

In the next case, in which the section was undertaken because of anaphylaxis, the physician stated in the questionnaire that the death was due to misgrouping. That, of course, may be true, but the question arises whether this death was not connected in some way with the recently discovered Rh factor.

In another case, intestinal obstruction may have been the correct cause of death. The cause as given in the questionnaire was "intestinal stasis, probable ulcer of the stomach." The patient had had three previous abdominal operations. The investigator found that she had given a history of chronic indigestion for several years. She had had vomiting and abdominal pain when seven months pregnant. She vomited a good deal after the operation. At operation, many adhesions were found, and the investigator believed that the death was in all probability due to intestinal obstruction, which was incomplete at the beginning and later became complete.

The indication for the last case, in which the cause of death was lobar pneumonia, was "elderly primipara." The patient was in labor for some hours. The questionnaire states that she developed lobar pneumonia and cardiac failure and died on the fourth day. No further information is available regarding this case.

It is difficult to say how many of these deaths were preventable, but I think it will be agreed that the number of deaths was greater than it should have been. There were 219 maternal deaths in Massachusetts in 1940, giving a death rate of 2.8. But it must be noted that cesarean section figured in nearly 19 per cent of the deaths. There is no doubt that the results obtained were remarkably good. However, the fact remains that altogether too many sections are being done.

In 1940, there was a greater variance between the statements on the questionnaires and the facts elicited by the investigators. It was obvious in some cases that the questionnaires covered up the actual causes of death and the indications for operation.

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THE TREATMENT OF PSORIASIS WITH A SARSAPARILLA COMPOUND*

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SARSAPARILLA has been used as a medicament since 1603, when Martin Pring,[1] in the English ship *Speedwell*, searched the New England coast for forests of sassafras, which then was considered "a panacea for all manner of disease." In America, the earliest colonial settlers purveyed sarsaparilla as the inevitable spring tonic, attributing to its use a diuretic, diaphoretic, tonic and alterative effect. By 1892, Schulz[2] recognized the fact that there were different varieties of this dried root of the Smilax species and believed that he had isolated three distinct saponins from sarsaparilla: parillin, sarsasaponin and smilasaponin. Since the observation of Schulz, a voluminous literature on the saponins has accumulated. It is the water-soluble saponin called sarsasaponin (parillin), obtained from the Honduras variety of sarsaparilla, that forms the active ingredient of the tablets used in this study.

A survey of the literature, covering fifty-two original articles, on the chemical composition of the various types of sarsaparilla, the nature of the saponins and the structure of the sapogenins reveals that only one definite saponin has been isolated from any of the varieties of sarsaparilla. This compound is generally called "sarsasaponin (parillin)." Its chemical constants are: melting point, 238 to 240°C. (Van der Haar[3]) and formula, $C_{45}H_{74}O_{17}$. On hydrolysis with dilute acid, it yields one molecule of sarsasapogenin (parigenin), two molecules of glucose and one molecule of rhamnose. The Honduras and Mexican varieties apparently contain no other saponins.

In sassafras and various other plants distributed throughout the botanical realm, one finds a group of compounds referred to as the "digitalis saponins (and sapogenins)." These digitalis saponins, of

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which sarsasaponin is one, are not to be confused with the "cardiac glycosides" obtained from digitalis plants. The term "digitalis saponins" is purely a chemical classification, and a confusing one at that. Chemically, the two substances are sharply differentiated. Each has quite different and characteristic side chains. The digitalis sapogenins have none of the physiologic action on heart muscle that characterizes the cardiac glysosides, which also contain unusual sugar molecules not found elsewhere in nature. A still further differentiation lies in the ability of the digitalis saponins to hemolyze erythrocytes in very low concentrations. The sarsasaponin product used in this study is prepared from a particular sarsaparilla and embodies no possibility of contamination with the digitalis cardiac principle; furthermore, the standardization of this sarsasaponin compound by the hemolytic index serves so completely to control optimal quality and uniformity of composition that hemolysis does not present a problem.

Ransom,[4] in 1901, in an out-moded way, demonstrated a chemical affinity between the saponins and serum cholesterin by which the saponins acted on tissues without causing hemolysis. This affinity of saponins for cholesterol led Deneke,[5] in 1936, to utilize the studies that Grütz and Bürger[6] had completed three years earlier. Grütz and Bürger found that patients with psoriasis (as compared with nonpsoriatic persons, showed an increase, respectively, in total blood fat of 44 per cent, cholesterol 33 per cent, and phosphatides 43 per cent. Following this, they naturally restricted the fat intake of patients with psoriasis. Deneke advanced farther, by supplementing the fat-deficient diet with the oral administration of sarsaparilla, hoping to utilize the chemical affinity of the sarsaparilla saponin for cholesterin. This procedure met with some success.

Not all patients with psoriasis, however, have a disturbed lipid metabolism. Hering,[7] in 1938, duplicating the work of Grütz and Bürger, observed that the phosphatide content of the blood approached normal levels, and that the free and esterified cholesterol showed no significant deviations from normal. Hering did not believe a relation existed between psoriasis and a disturbed metabolism of fats. Rosen et al.,[8] in 1937, concluded that the psoriatic process involves hypocholesteremia rather than hypercholesteremia; moreover, on the basis of cholesterol-tolerance tests, the author asserted that it is not possible to assume that a disturbance of lipid metabolism is present in patients with psoriasis. Grubb,[9] in 1935, assuming psoriasis to be a deficiency disease in which the vitamins of animal fats were lacking, prescribed a diet rich in butter (fat) for 3 patients in whose diets butter had been previously prohibited, and the psoriasis disappeared in a short time. Madden,[10] in 1939, using cholesterol-tolerance tests, observed that hypercholesteremia did not generally exist, but that a low-fat diet was of definite value in 68 per cent of cases tested. Madden's patients were hospitalized. He inclined to the belief that the favorable effect of diet might be explained on the basis of a general realignment of metabolism, rather than because of the correction of a disturbed fat metabolism. He asserted that sarsaparilla, because of its saponin content, has an especial affinity for cholesterol and that its ingestion tends to restrict excesses. Stewart et al.,[11] in 1939, observed in 6 cases of psoriasis, that 3 patients had lipemia, 2 had blood-lipid values within normal range, and 1 showed subnormal values. Despite these conflicting observations, Wise and Sulzberger[12] state that there is no doubt that certain cases of psoriasis are much improved by a strict "fatless" diet. Their special article on psoriasis and its treatment is an excellent contribution, and should be read by all who are interested in this disease.

To Philippsohn[13] should go the credit for modernizing the old observation that sarsaparilla possessed value as a medicine. His successful use of sarsaparilla in the treatment of psoriasis is interesting. Patients were instructed to make their own compound. Into 1000 cc. of tepid water, 15 gm. of sarsaparilla was placed. This was done in the afternoon, and the mixture was allowed to stand overnight, and then boiled for twenty minutes the following morning. While the mixture was still hot, the patient drank half the liquid that morning, the remainder being consumed during the afternoon of the same day. Usually after a week of this daily procedure, decreased desquamation occurred, which, after its complete disappearance, was marked by a smooth red macule that eventually faded. Philippsohn noted no untoward effect from sarsaparilla. One patient who had used the mixture daily for twenty years failed to experience a single relapse of a previously stubborn psoriasis.

Ritter,[14] using the sarsaparilla tablets of Bürger, treated 19 private patients. Ten tablets were administered daily. Nine patients became completely or nearly completely free from psoriasis. The shortest required duration of treatment was two weeks, the average period being sixty to one hundred days. Five cases showed improvement but did not completely clear. Five patients showed no improvement at all. On the 10 patients without satisfactory response, Ritter also used a low-fat diet, bland ointments, salicylated vaseline, precipitates and chrysarobin. No harmful or toxic effects were observed.

Zaun,[15] in 1938, treated 20 cases of psoriasis, using five to thirty sarsaparilla tablets daily, a low-fat diet and a salicylated ointment locally. Satisfactory results were obtained in all cases except a few in which the patients failed to follow treatment as advised.

Wise and Sulzberger[12] describe the use of sarsaparilla tablets as a treatment for psoriasis. Baird[16] comments conservatively on the results obtained in 6 cases treated with sarsaparilla.

With an appreciation of the facts as outlined above, there appeared a certain logic in the thought that the standardized, nontoxic, water-soluble fraction of sarsaparilla (sarsasaponin) should possess virtues in the treatment of psoriasis. The present communication is a report of such a study.

Clinical Material

This clinical study covers the past two years. A two-year period was deemed necessary because of the desirability of studying the effectiveness of sarsasaponin tablets on the seasonal variations of psoriasis and its efficacy in controlling recurrent eruptions.

Ninety-two patients were studied. Of these, 75 were treated with the sarsasaponin tablets, and 17 were used as controls. Twelve additional cases were started, but failed to continue a sufficient period to merit inclusion in the series. There were 53 females and 39 males, a ratio of 1.3:1. The average age of onset was twenty-nine years. The youngest patient was three years of age, and the oldest seventy-six. The earliest age of onset was infancy, and the latest sixty-seven. The average duration of psoriasis was ten years, the shortest being three weeks, and the longest fifty-two years. Thirty-seven patients had psoriasis ten years or longer.

A history of familial incidence was obtained in 15 cases (16 per cent). The parents of 5 patients had psoriasis. In contrast, 53 (20 male and 33 female) were the parents of 121 children, and in no case did psoriasis appear in their progeny. This observation indicates clearly that psoriasis is not a deterrent to marriage and the begetting of progeny. Third-generation psoriasis was not noted. The patients were American, English, Canadian, Scottish, Irish, Swedish, Russian, Lithuanian, Portuguese, Jewish, German and Italian.

Objectively, the lesions were of the type and distribution generally described as psoriasis vulgaris. Arthritis or rheumatic joint disease was present in 13 cases (14 per cent). There were no cases of psoriasis pustulosa. Characteristic polymorphism of the lesions was apparent. Large plaque-type lesions were present in 42 per cent. Expressed in percentage, the following areas were involved: scalp, 74; trunk, 60; elbows, 60; knees, 53; nails, 32; genitals, groins and gluteal crease, 36.

The subjective symptoms of itching and burning at one stage or another were unusually frequent, being present in 68 per cent of the cases. Nervousness, a tendency to worry, and vasomotor instability, which, when acute, accentuated pruritus and frequently stimulated the appearance of new crops of lesions, were noted in 36 per cent. A seventeen-year-old boy, brooding over his psoriasis, made four attempts at suicide. One patient, on the death of her husband, quickly developed a fresh exanthematous spread of new lesions. One patient, a student at a local university, was also a student aviator. Owing to storms and bad weather, there was no flying in February, and his psoriasis began to clear. Then came the time for his first solo test flight. Apparently, the nervousness and excitement in anticipation of this examination proved sufficiently stimulating to cause improvement of the lesions to cease, and his psoriasis became quite active and more widespread.

There were several examples of polysensitivity among these cases, such as asthma, hay fever, urticaria and eczema, which had occurred in antecedent members of the patient's families, although a family history of psoriasis was not necessarily present.

The histories in 85 per cent revealed a distinct tendency for the psoriasis to improve during the warm summer months. All patients were warned about overexposure to the sun, yet, in 5 cases of severe sunburn, fresh outbreaks of punctate, guttate or nummular lesions occurred. In New England, the predominant periods for recurrent eruptions are September and October, and March and April, whereas during the winter, when skins and scalps are dry, nails are brittle, and seasonal keratotic follicularis is marked, the psoriatic patient is hard pressed. The patient with psoriasis apparently has a peculiar inherent physiologic habitat on which any number of factors and circumstances may prove stimulating, and when present in sufficient force the inevitable cutaneous response is one of psoriasis.

In all cases, syphilis was ruled out as an etiologic factor, either by treatment or by physical examination and negative Hinton, Wassermann and Kahn reactions of the blood. In 4 cases in which syphilis was present, it was of the tertiary type, and treatment did not influence the psoriasis, except occasionally to produce an accentuation of the lesions. A careful check was kept on the renal status and the hemoglobin and blood counts all through this study. In no case was there evidence of renal irritation. Blood counts performed before, during and following treatment with the sarsasaponin tablets failed to reveal evidence of hemolysis. Three patients showed a rise in hemoglobin from 10 to

15 per cent. The erythrocyte count either held its level determined prior to treatment, or showed an increase of as much as 750,000 cells. The leukocyte count seemed unaffected. The differential counts were not remarkable except for a fairly consistent though mild eosinophilia. The blood smears invariably revealed a goodly number of platelets in all preparations.

Treatment

Dosage

It is essential that the sarsasaponin tablets be taken regularly. It is advisable, at the start, to prepare the patient for a three to seven months' course of the medication. If a shorter period is required, so much the better.

The usual adult dose is one tablet* twice daily, preferably taken with a warm liquid at a time when the stomach is likeliest to be empty. These two periods are the early morning on arising and the last thing at night before retiring. A larger dose, two tablets twice daily, or even two tablets morning and evening and one at noon before luncheon, may unhesitatingly be administered. For children aged five years or under, half a scored tablet given twice daily is sufficient.

A diet low in fat will prove beneficial for a large number of patients. Liquids in the amount of 1500 cc. or more daily are recommended.

It should be stated that, for the purpose of this investigation, the tablets used were less concentrated than those that are commercially available at present. A single tablet of the dosage described above contains the equivalent amount of sarsasaponin contained in five of the tablets used in the clinical evaluation. This concentration of the active ingredient of five of the old tablets into one of the new tablets was considered advisable merely as a convenience for the patient. The new tablet is scored; the smaller and older tablet is not. All statements regarding the sarsasaponin tablets in this paper, therefore, apply to the smaller, older tablet of weaker strength. Its equivalent in new tablets may be obtained by dividing by five.

Local Therapy

During the first twelve months of this study, no diet or topical applications were prescribed. During this period, it was shown that the tablets were nontoxic and therapeutically effective. With these two points cleared, there could be no logical objection to a local therapy designed to hasten involution of the lesions, provided that this therapy was not irritating. Consequently, a variety of topical applications were used. They comprised, chiefly: irradiation in the form of sunshine or ultraviolet lamp, boric acid ointment, lanolin, petrolatum, olive oil, mild precipitate ointments, salicylic and sulfur preparations, and modified coal tars. Of these, the most effective agents were irradiant energy and a modified coal-tar preparation, Ultroine Ointment.† This ointment is a clean, gray to white, nonirritating preparation, which has as its active ingredient the distillate of coal tar. The 2.5, 10 and 20 per cent concentrations proved exceedingly beneficial as a topical application twice daily. One can state definitely that the oral administration of the sarsasaponin seemed to enhance the effectiveness of treatment locally.

Results

Table 1 shows that in the group treated with the sarsasaponin tablets there was a satisfactory improvement, as compared with the condition of the controls. By combining the results of moderate and marked improvement, the percentage that may be considered good was 62. Eighteen per cent of cases cleared completely. The data on improvement compares favorably with Ritter's[14] experience in 19 private patients treated with the sarsaparilla tablets of Bürger. Nine of Ritter's patients (48 per cent) became completely or nearly completely free of psoriasis, 5 (26 per cent) showed some improvement, and 5 showed no improvement.

Table 1. *Results of Treatment with Sarsasaponin Tablets.*

Results	Treated Cases		Control Cases	
	Number of Patients	Per-cent-age	Number of Patients	Per-cent-age
Clearance (100%)	14	18	1	6
Marked improvement (75%)	16	21	1	6
Moderate improvement (50%)	17	23	2	12
Slight improvement (25%)	12	16	3	18
No improvement	14	19	7	41
Exacerbation of lesions	2	3	3	17
Totals	75		17	

In the 14 cases that cleared, the average period of treatment was four months; the shortest period was four weeks, and the longest seven months. The average period of remissions was eight months, the shortest being three months and the longest twenty months. An analysis of these cases reveals that the greatest clearing occurred during the late spring and summer (Table 2). The experience of two full summers showed no photosensitive effect from the sun. As a matter of fact, there is a distinct impression that the tablets enhance the effectiveness of mild sunshine.

Forty per cent of the patients showed moderate or marked improvement. Most of them also

*The sarsaparilla (Sas-Par) tablets used in this study were supplied by Ernst Bischoff Company, Incorporated, Ivoryton, Connecticut.

†This mixture is manufactured by Lanyard Chemicals, Incorporated, Boston.

showed the greatest benefit during the warm summer months. This cannot be entirely attributed to the direct effect of the sun's rays, because many of the patients had indoor occupations and little or no opportunity for beach or sun bathing. There is something about the warmer seasons of the year that is beneficial to psoriasis.

Recurrent eruptions most commonly appeared in the fall, winter and spring. Although the administration of this sarsaparilla saponin did not completely control these recurrences, their intensity was considerably modified and less severe as compared with similar periods of cold weather during

TABLE 2. *Analysis of 14 Treated Patients Whose Psoriasis Cleared.*

TOTAL PERIOD OF TREATMENT	NO. OF TABLETS REQUIRED	PERIOD OF TREATMENT	RECURRENCE OF PSORIASIS	LENGTH OF REMISSION
MONTHS				MONTHS
1	225	February	January	11
2	525	June–August	May	9
2	600	June–August	December	4
2	825	April–June	None	10
3	600	October–January	July	6
3	975	February–May	September	4
3½	525	April–July	None	12
4	1425	February–June	October	4
4	1800	February–June	February	8
5	1650	November–April	None	20
5½	1650	February–July	December	5
6	1250	May–November	None	3
7	2325	October–May	September	4
7	2416	November–June	None	18

preceding years. The dissemination of the eruption was less widespread, its course was milder, the response to local therapy was better, and itching was not nearly the uncomfortable factor that it had usually been. In many cases, the control of pruritus was dramatic. In others, itching was intense, regardless of what was used.

Of the 13 cases of arthritis or rheumatic joint disease and psoriasis, nothing definite can be said about relief of pain. One patient, a sixty-six-year-old man, had painful arthritic involvement of the wrists, hands and right ankle; he received 2925 sarsasaponin tablets over a nine months' period, and it was not until the last three months (October, November and December) of treatment that relief from pain and improvement of the psoriasis were obtained. A forty-three-year-old woman had severe generalized psoriasis including the scalp and nails, and nodular painful arthritic deformities of the hands. She took 5900 sarsasaponin tablets for twenty-one months. The arthritis and psoriasis, including the scalp and nails, were markedly improved. She gained weight, the psoriasis underwent two almost complete remissions, and during the past winter her arthritic pains and psoriasis were so slight as not to be noticeable. She continues to take the sarsaparilla tablets. Another patient, a seventy-six-year-old woman, had painful arthritis and a chronic, generalized, plaque and papular psoriasis of twenty-two years' duration. The scalp, nails, genitals and gluteal crease were also involved. Her greatest relief was obtained from the sarsasaponin medication. In twenty-two months, this patient took 6075 tablets, and, although the psoriasis was not completely controlled, improvement was moderate, and she continued to take the sarsaparilla compound. In contrast to these favorable impressions, there were similar cases in which the arthritic pains and psoriasis continued apace despite the saponin medication.

Twenty-six cases (35 per cent) of the series showed slight to no improvement, and in 2 (3 per cent) the psoriasis was distinctly accentuated. Thus, in 38 per cent, the response was not favorable. In the light of present knowledge, no adequate explanation for this failure may be advanced. The average period of treatment was three months, and the average number of tablets administered was 942. If this group is contrasted with the successful cases, which required an average of four months to establish a remission, a fair trial period of the tablets is three or four months.

A typical case with complete remission is that of a thirty-two-year-old man. His psoriasis was of eighteen years' duration and generalized—in fact it was so severe that he went outside only at night. There was slight improvement from sun bathing and the use of an ultraviolet lamp, but at no time was there complete clearing. In November, 1939, the patient began sarsasaponin, taking five tablets twice daily. A low-fat diet was advised, and no local therapy was prescribed. Within two weeks, there was a noticeable reduction in the eruption, and pruritus was controlled. The dosage was increased to eight tablets twice daily. Within the next four weeks, the scalp was greatly improved, the scalp hair regained a natural waviness and luster, and the previously extensive eruption on the face was indicated only by erythematous macular patches. Within ten weeks from the start of this medication, only a few patches of psoriasis remained on the arms, chest and thighs. In February, a slight exacerbation of the eruption occurred. At this time, the patient had been without the tablets for a week. On resumption of sarsasaponin, the new lesions quickly vanished, and favorable progress, although slower than at first, was steady. By June, 1940, seven months later, there was no trace of the psoriasis. All areas, including the scalp, groin, elbows and knees, were completely clear.

The effect of a low-fat diet seemed to be helpful. Twenty-four patients were advised to eat as little fatty food as possible during the period of treatment. Of these, 50 per cent showed marked im-

provement, and 16 per cent, complete clearing, whereas the remaining 34 per cent were either slightly improved or less. There can be no doubt that certain cases of psoriasis are improved by the use of a low-fat diet.

The results attained by the use of the saponin of sarsaparilla were superior to those with the usual procedures commonly applied in the 17 patients used as controls. Table 1 amply illustrates this point.

The control cases received dietary management; local treatment, such as Alpine sun lamp, cold quartz ultraviolet radiation, sunshine and ointments of various kinds, including salicylic acid, sulfur, precipitates and coal and wood tars; colloidal manganese, bismuth and liver extract intramuscularly; arsenic in the form of Fowler's solution; and vitamins A, D and B complex orally.

Discussion

The results attained in this series of 75 treated cases of psoriasis were neither remarkably successful nor disappointing. They were far better than average. In certain cases, they were brilliant. Emphatically, sarsasaponin is worthy of clinical trial in any case of psoriasis. No toxic systemic effect from its use was observed. A careful check on the cardiovascular, renal, gastrointestinal and hematopoietic systems failed to reveal any untoward reaction. In contrast, many of the patients developed increased appetite, gained from 4 to 12 pounds in weight, and seemed less nervous, slept better and experienced less itching. Three women took the sarsasaponin during pregnancy without ill effect, and their psoriasis simultaneously improved.

One distinct impression regarding sarsasaponin therapy is that the drug has a greater value in clearing the chronic, large, plaque type of lesion than it has in controlling the recurrent evanescent and exanthematous punctate, nummular and guttate lesions. The individual new recurrent crops of eruption, in most cases, were milder, but they did appear despite the sarsasaponin medication.

These cases gave rise to the impression that vasomotor instability, blond complexion and a tendency toward anxiety, worry and nervousness are not causative or even predisposing factors to the occurrence of psoriasis, but that psoriasis runs a more recalcitrant course in a person possessing this triad.

The tragic and conditioning features of psoriasis on the behavior of this small group is illustrated by one suicide, one attempt at suicide, two adolescents with mental reactions of inferiority that led to strange and perverted behavior, several cases of refusal to marry, and numerous patients with neuroses because of their disfigured appearance.

Summary and Conclusions

A new drug, the water-soluble saponin, called "sarsasaponin (parillin)," obtained from Honduras sarsaparilla is described. The technic of its administration and its effectiveness in 75 patients with psoriasis are discussed. Seventeen additional cases served as controls. The study covered two years.

Observations from the literature concerning the nature of the sarsaparilla saponins and the influence of lipid metabolism on psoriasis are made.

When administered orally, the sarsaparilla tablets had a decided and beneficial effect on 62 per cent of patients with psoriasis.

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A MECHANISM FOR SYNCOPAL ATTACKS ASSOCIATED WITH PAROXYSMAL AURICULAR FIBRILLATION

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FROM a clinical standpoint, the mechanism of attacks of faintness or of actual syncope may be extremely obscure even after considerable study, since observation of the attack is often necessary to clarify the problem. In patients with rather infrequent attacks, such observation is entirely fortuitous unless they can be produced at will, and consequently the primary mechanism of the seizures usually remains a matter of speculation. Contrary to popular belief, organic heart disease is an uncommon cause of syncope, and such cases are confined largely to ventricular arrest due to interference with the conduction system as a result of coronary-artery disease and to the even rarer syncopal attacks associated with aortic stenosis or the shock of severe coronary insufficiency.

It is known that exaggerated vagal reflexes can cause functional disturbances in the regulatory mechanism of the normal heart, resulting in ventricular or complete cardiac arrest, and can thereby produce cerebral ischemia and syncope by a secondary lowering of the blood pressure. The sensitive carotid sinus, for example, at times acts in this manner to produce fainting. Furthermore, it is known that vagal stimulation may be a factor in precipitating auricular fibrillation.

It has been recognized for many years that faintness and syncope may be associated with attacks of the various paroxysmal arrhythmias. Although usually attributed to a drop in blood pressure consequent to the rapid ventricular rate, I believe the primary mechanism responsible for syncope in these cases has never been adequately demonstrated. The chance observation of the following case during a syncopal attack throws new light on a mechanism producing syncope in some of these cases.

CASE REPORT

G. H. B., a 40-year-old married male nurse, was first seen in February, 1941. Since 1932, his usual good health had been periodically marred by attacks of faintness or syncope followed by short bouts of palpitation and irregular heart action. While feeling well and for no apparent reason, the patient experienced attacks of faintness or loss of consciousness of several minutes' duration, following which he was aware of irregular heart action that ceased abruptly within 30 minutes to several hours. Other than causing some heart consciousness, the palpitation was not particularly uncomfortable and produced no ill effects. To the patient's knowledge, no convulsions had ever been associated with the syncopal seizures. These attacks usually recurred for a day or so and then disappeared for periods varying from several months to several years. Since the onset, six or seven episodes had occurred, the last in 1938, following which the patient had consulted a cardiologist, who had found no physical abnormalities. Lumbar puncture, the Wassermann reaction, blood-sugar curves, the basal metabolic rate and electrocardiograms had always been normal.

The present episode, typical of those in the past, had started 36 hours previously, during which the patient had had several attacks of faintness and one attack of syncope. While the patient was being examined, he suddenly stated that an attack was coming on, and loss of consciousness gradually supervened, with progressively increasing ashen pallor, eyes at first staring and then rolling upward, and a cold clammy skin. The heart sounds, which had previously been audible and regular, ceased (no auricular sounds were heard), and asystole continued for at least 15 seconds, following which three or four slow irregular beats — at intervals of 2 or 3 seconds — were heard; gradually, an irregular rhythm was established at approximately 80 beats per minute, and consciousness returned. Afterward, the patient had no complaint except for irregular palpitation and a feeling of weakness. This bout of palpitation lasted about 3 hours and then ceased abruptly. When the patient was seen 3 days later, there had been no further attacks, and the attack observed was apparently the last of the present series.

The electrocardiogram taken during the irregular rhythm showed flutter fibrillation, with occasional ventricular ectopic beats at a ventricular rate of about 85 beats per minute (Fig. 1). The electrocardiogram taken 3 days later was entirely normal (Fig. 2).

Complete physical examination and fluoroscopic study of the heart and lungs several days after the attack showed no abnormality. The carotid sinus was not unduly sensitive.

It is of some interest that the sequence of events in this case parallels the findings of Iglauer, Davis and Altschule† and others who have induced auricular fibrillation in normal animals by vagal stimulation. It has been observed that auricular fibrillation, when produced experimentally by vagal stimulation, is not infrequently preceded by a short period of heart block; in a dog in which fibrillation was prolonged, the ventricular rate was slow. The ventricular rate of paroxysmal auricular fibrillation in human subjects is usually quite rapid (125 to 150), and it is therefore worth noting that in the case presented the ventricular rate averaged only 85 beats per minute. Exactly what type of heart block occurred is unproved, since good fortune did not extend itself to the point of allowing an electrocardiographic registration of this period.

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†Iglauer, A., Davis, D., and Altschule, M. Auricular fibrillation in normal, intact animals after the intravenous administration of Mecholyl. *Am. Heart J.* 22:47-55, 1941.

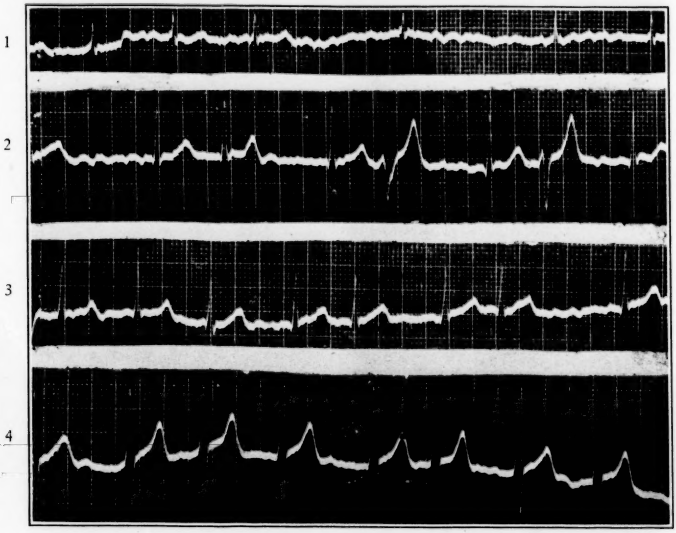

FIGURE 1. *Electrocardiogram during Paroxysmal Auricular Fibrillation.*

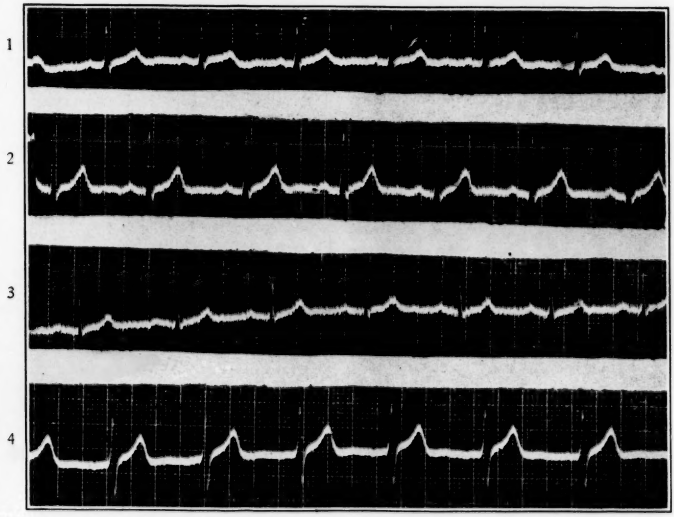

FIGURE 2. *Electrocardiogram during Normal Rhythm.*

It seems probable, however, that complete cardiac arrest (sinoauricular block) occurred rather than auriculoventricular block with only ventricular arrest. In any event, it seems but a short step from cardiac standstill caused by a vagotonic influence to auricular fibrillation due to the same mechanism.

Discussion

It is also of interest to carry to the auricles the analogy of the events known to occur in the ventricles during Adams–Stokes seizures associated with complete auriculoventricular block, in which syncopal seizures are likeliest to occur during the paroxysmal stage of complete heart block; once the block is permanently established, the fainting attacks usually disappear. It has been shown electrocardiographically that there is frequently a latent period, with complete ventricular arrest and a syncopal attack, between the cessation of normal rhythm and the establishment of an idioventricular rhythm. It is possible that in the case presented above a similar latent period affecting the auricles, with consequent cardiac arrest, occurred between the cessation of activity in the sinoauricular node (sinoauricular block) and the establishment of auricular fibrillation. Since a common interpretation is that the paroxysmal auricular arrhythmias are due to auricular irritability, it may be that in some cases these arrhythmias represent an auricular escape as a result of a depressed sinoauricular node instead of the commoner ventricular escape. Depression of the sinoauricular node is usually functional and the result of vagal activity, although there is some evidence that in older patients the node may be depressed as a result of impaired circulation due to coronary-artery disease.

Of the two possible mechanisms discussed above, the former appears to rest on a sounder experimental foundation and seems the more probable. Both, however, are purely speculative so far as the present case is concerned.

Conclusions

Faintness and syncope associated with some cases of paroxysmal auricular fibrillation may not be due to a fall in blood pressure and cerebral ischemia as a result of a rapid ventricular rate but rather to asystole during a latent period between the cessation of normal rhythm and the establishment of the auricular arrhythmia. Either the cardiac standstill or the auricular fibrillation, or both, may be of vagotonic origin.

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MEDICAL PROGRESS

PHYSIOLOGY*

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Surgical Physiology

NO SMALL part of medical progress arises from the attempt to express the changes taking place in disease in terms of the physical sciences and it is no longer necessary to defend the advantages of a scientific training as a basis for a career in medicine. One of the more interesting indications of the popularity of this trend is the appearance of books that purport to interpret to the practicing physician one of the basic sciences involved in his specialty. One remembers Hewlett's *Pathological Physiology of Internal Disease* as an earlier work of this kind. Peters and Van Slyke's *Quantitative Clinical Chemistry* is without question the model for all subsequent attempts, and establishes criteria by which they must be judged.

The first essential of a book of this kind is that the material it presents and the statements it makes should, so far as possible, be correct, or should represent the result of a rational criticism of available data. Secondly, the applicability to man and to the specialty of the material presented should be most carefully scrutinized. Thirdly, the author should take pains to point out subjects in need of clarification, and should facilitate more extended study by careful documentation at every point. Finally, there is the requirement of completeness of coverage, not demanded in a monograph, but essential in a book of this type.

Judged by such rigorous standards, a recent volume, *Surgical Physiology*, by Nash[1] falls somewhat short of expectations. There seem to be no gross errors in fact, but a number of minor flaws can be seen, such as the statement (page 34) that

Reprints of articles in this series are not available for distribution, but the articles will be published in book form. The current volume is *Medical Progress: Annual, 1940* (Springfield, Illinois: Charles C Thomas Company, 1941. $4.00).

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ordinary fainting attacks are "largely due to vagal slowing of the heart." An example of uncritical handling of material is the discussion (page 43) of plasma potassium in shock without reference to the physiologic effects of potassium, or the possible toxic effects of an elevation of plasma potassium. A typical example of failure to consider the applicability to man of physiologic data is the assertion (page 5) that "experimentally an excess of calcium ions causes standstill of the heart in extreme systole, a condition known as 'calcium-rigor.'" This phenomenon occurs in the frog and turtle heart, but not in the mammalian heart, in which ventricular fibrillation or arrest without rigor may be the terminal event. The bibliography is limited, and not in a very useful form, and most statements are without documentation. Among the problems dealt with inadequately or not at all are the cardiovascular complications in anesthesia, the lymphatic system and the clotting of blood.

There is perhaps another way of judging this book. It does present material that is rather widely diffused in the literature, and thus serves as a compact and ready source of the salient points of many a subject.

A surgeon with ready access to a well-kept library would probably be better satisfied to consult, first, Wigger's *Physiology in Health and Disease*, Best and Taylor's *The Physiological Basis of Medical Practice* or — what in my opinion is still better — Bard's *Physiology in Modern Medicine*, and then to continue the subject in a specialized monograph like Peters's *Body Water* or Salter's *The Endocrine Function of Iodine*. Finally, he could work through the specialized reviews in journals into the original articles. Surgeons not so fortunately situated will find Nash's volume of considerable assistance in reaching an understanding of the physiologic basis of their surgical problems.

Role of Veins in Syncope and Shocklike States

Sudden collapse after what may have been a trifling injury, or following an unexpected fright, is a phenomenon commonly enough observed but surprisingly little understood. Lewis,[2] who described the condition in soldiers, termed it a "vasovagal collapse," being impressed by the slow pulse so frequently seen, and by the supposed value of atropine in its therapy. Later studies demonstrated that atropine did prevent the slowing of the pulse but did not influence the collapse, and Lewis pointed out that the vagus nerve was therefore not vitally concerned in the phenomenon, which presumably then implicated the vasomotor system. It is, of course, largely to the credit of Weiss[3] that a collapse syndrome was defined in which the vagus nerve is basically responsible. Despite such a clear separation of the two conditions, one continues to find references to the vagal origin of the so-called "vasovagal syndrome," and to the necessity for atropine as a prophylactic or therapeutic measure.

The next major advance in the elucidation of the vasovagal syndrome, to which the term "primary shock" might also apply, was also made by Weiss.[4, 5] Although clinicians and physiologists described the phenomenon in vague terms of "vasomotor paralysis" or "splanchnic vasodilatation," Weiss was able to demonstrate that the locus of the circulatory disturbance is in the veins and venules, and possibly the capillaries, whereas the arterial tree shows, if anything, a vasoconstriction. In other words, the fall in blood pressure is due, not to generalized peripheral vasodilatation, which reduces the peripheral resistance to a degree where blood escapes from the arterial system so rapidly that a head of pressure cannot be maintained, but rather to the fact that the veins and venules dilate greatly and act as a reservoir for large amounts of blood. Venous pressure at the right auricle then falls, cardiac filling diminishes, and concomitantly, cardiac output and arterial blood pressure decrease. Later studies of a slightly different type (venous occlusion by ligature) indicate that the pooling of about a liter of blood is sufficient to induce symptoms of collapse.[6]

The experiments of Weiss involve the interaction of two factors: the upright posture on a tilting table, which reduces muscular activity in the dependent parts of the body, and the administration of small doses of sodium nitrite. Either procedure alone usually produces no symptoms, but the combination regularly induces the typical syndrome in which "the primary change consists in tachycardia, small arterial pulse pressure, with small pulse volume (thready pulse), fall in the venous pressure, and arteriolar vasoconstriction." Studying the cause of the fall in venous pressure, Weiss and his collaborators found that nitrites cause a profound diminution in the tone of the venous system, so that, to raise the venous pressure in a limb to a given level, far more blood would have to flow into the vessels of the part. The rate of inflow is diminished, indicating the presence of arteriolar vasoconstriction. In the absence of the muscular massage that normally promotes the emptying of veins toward the heart, such dilatable veins could not resist the force of gravity which tends to pool blood in dependent parts.

Inquiries emphasize the fact that therapeutic or prophylactic measures must be taken primarily to increase venous pressure. Restoration to the horizontal position is always rapidly effective. Larger doses of nitrites can cause collapse, even in the horizontal position, and elevation of the lower

part of the body is presumably an effective therapy. The common vasoconstrictor drugs — epinephrine and Pitressin — are without value, and Pitressin probably facilitates collapse.[7, 8] Paredrinol (*a-n*-dimethyl-*p*-hydroxphenethylamine) was shown to be distinctly useful in a number of cases, either preventing collapse completely or greatly delaying its onset.[9] This substance, first studied by Rein,[10] has a more active vasoconstrictor influence on the venous than the arterial portions of the circulatory system.[12, 13]

Search is now being made for situations in which a similar loss of venous tone forms the basis for other shocklike phenomena. Paredrinol appears to be effective in severe cases of postural hypotension with syncope and is occasionally of value in the hypotension associated with acute infectious diseases. A decreased venous tone and the presence of postural syncope have been reported during the convalescent stages of such illnesses.[13–15] Careful studies by Ebert and Stead,[16] however, reveal that this is not the only, perhaps not the paramount, circulatory disturbance during the acute stage of infectious diseases, since elevation of the feet and intravenous infusions of whole blood, plasma or 10 per cent glucose fail to produce improvement in the circulation. The patients in whom these procedures were tried were virtually moribund, and in certain cases, elevation in blood pressure was evoked. It must also be recalled that Altschule and Gilligan[17] and others[18] have demonstrated how very quickly even large transfusions are compensated for by vasodilatation that includes arteriole and venuoles, so that only temporary changes in blood pressure are to be expected.

Denny-Brown and Russell[19] offer evidence, which cannot be said to be completely convincing, that pooling in the venous system is responsible for the initial fall in blood pressure after concussion caused by blows on the head. They suggest "vasomotor paralysis" or stimulation of the glossopharyngeal-vagal mechanism as the responsible factor. These suggestions demonstrate how little is yet known of the pathologic physiology of the veins. From Franklin's[20] review of the data up to 1937, it appears that the veins of the abdomen are normally innervated by fibers of the sympathetic system; that section of these nerves dilates the veins, whereas stimulation of the peripheral stump of the nerve constricts them; that after ergotoxine to paralyze sympathetic hormonal effects, stimulation of the same nerve causes venous dilatation; and that the dilatation of the veins produced by tapping of the vein or the abdomen is a local effect not dependent on the central nervous system. At that time, Franklin could not find any circumstances in which reflex venous dilatation had been demonstrated without question. The value of continuation of the studies inaugurated by Weiss is obvious.

Renal Blood Flow in Human Hypertension

The method of Diodrast clearance, which Smith and his colleagues[21] have shown to measure blood flow through the excretory portions of the kidney, has now been applied to a study of blood flow in human hypertension. These studies indicate clearly that a reduction in renal blood flow, which occurs in so-called "essential hypertension" may be of extreme degree.[22–24] The administration of a pyrogenic substance (inulin), which causes an increase in renal blood flow in the normal kidney, has the same effect in the hypertensive kidney. Such findings are consistent with the view that in such kidneys, a reversible vasoconstriction exists, perhaps in the efferent vessels of the glomerulus. The same studies detect a variable decrease in the total excretory mass, denoting a destruction of kidney substance. In no case of essential hypertension was it possible to detect any difference between the degree of involvement of the two kidneys.[25] In a study of 5 patients with hypertension associated with unilateral renal damage, a marked difference in the blood flow in the two kidneys was detected, although the blood flow in the supposedly normal kidney was also below normal.[26] Removal of the diseased kidney was followed in all 5 cases by an increase in the blood flow in the remaining kidney. A significant fall in blood pressure took place in 3 of the 5 patients, but in none was a normal blood pressure re-established, although in 3 cases a normal blood flow was established in the remaining kidney.

An unexpected finding is that in the hypertension of toxemia of pregnancy, in the pretoxemic state, or in the hypertensive state following toxemia of pregnancy, no indication of diminution in renal blood flow can be demonstrated.[27–30] Some evidence of increased blood flow is occasionally made out. These experiments cast certain grave doubts on any theory that explains all types of hypertension in man on the basis of renal ischemia. They do not, however, necessarily indicate that the hypothesis of a renal origin of hypertension need be abandoned. Corcoran and Page[31] call attention to the fact that dogs showing hypertension in response to renal arterial obstruction may also give normal Diodrast clearances. The persistence of experimental renal hypertension in the absence of renal ischemia is consistent with their view that intrarenal reduction of pulse pressure, rather than ischemia, may be the effective cause of experimental renal hypertension. The renal origin of the hypertension of toxemias of

pregnancy therefore still remains a possibility. The diminished renal blood flow in essential hypertension, of course, is also consistent with the renal origin of the disease, but there remains the possibility that the reversible vasoconstriction observed is only the renal manifestation of the generalized vasoconstriction that maintains the hypertension.

Induction of Ventricular Fibrillation

In man, ventricular fibrillation most frequently occurs as a sequel to an idioventricular tachysystolic episode. Several important factors in its origin have been pointed out, such as the facilitating influence of adrenalin or sympathetic stimulation in light chloroform anesthesia or acute benzol poisoning and that of intraventricular block in the fibrillation of heart disease. Recently, Wiggers and his co-workers[32-35] have analyzed in some detail the fibrillation occurring after single intense electrical shocks, after a series of induction shocks, and after anodal and cathodal polarization. In all these circumstances, it appears that a sequence of ventricular extrasystoles is set up, comprising in fact a short run of ventricular tachycardia in which all beats originate from the same focus. These impulses are at first conducted radially away from the point of origin and involve the entire ventricular mass. Each successive beat arises after a slightly reduced interval, and is conducted away from its site of origin. After a very few beats, one wave is found to be traveling only a centimeter or two behind the previous beat. At this point, two alternative events may occur: the next beat meets refractory tissue in all directions and is blocked completely, or block is irregular, and some avenues are still open to it. In the latter event, the stage is set for the establishment of so-called "circus motion," which constitutes ventricular fibrillation.

The intense single shock or the polarizing currents appear to create the initial series of tachysystoles by causing failure of the normal accommodation to internal or external stimuli, but obviously any tachysystoles may ultimately lead to ventricular fibrillation. Whether or not ventricular fibrillation develops must depend in the main on the state of the intracardiac conduction system. Any factors favoring the irregular development of intraventricular block must promote fibrillation, as Davis and Sprague[36] pointed out in 1928. Wiggers's theory seems to be essentially the same as that proposed by Nahum and Hoff[37] to account for the development of fibrillation by an intravenous injection of potassium chloride. These authors were impressed by the fact that fibrillation did not take place if marked reduction of cardiac rhythmicity occurred concomitantly with the development of intraventricular block, whereas fibrillation did occur if rhythmicity were maintained while block developed. They concluded that for the genesis of ventricular fibrillation two factors were essential: the presence of foci of automaticity in the ventricles, and intraventricular block. It is apparent that in the presence of an automatic focus of increasing rhythmicity, fibrillation may begin because of physiologic blocking in an otherwise normal heart. On the other hand, a heart in which damage to the myocardium has produced regions of varying block should be more susceptible to fibrillation than a normal heart. In a preliminary communication, Harris et al.[38] have extended their observations to include the fibrillation following occlusion of a coronary artery, and find a similar mechanism operating.

Coagulation of Blood

The so-called "classic theory" continues to retain validity as the basic explanation of blood coagulation. The reaction in two stages of prothrombin, calcium and thromboplastin to form thrombin, and of thrombin and fibrinogen to form fibrin, has been the subject of repeated examination. Although no insurmountable obstacle to its continued acceptance has as yet appeared, much has been learned of the nature and source of the individual factors, and of their role in the various hemorrhagic diseases. Excellent reviews by Quick[39] and Howell[40, 41] deal particularly with this problem.

The role of vitamin K in the production of prothrombin is now well recognized and needs no further review. An equally promising field, now in the stage of active development, deals with the nature of the thromboplastic substance. The recent significant contributions in this field are largely those of Taylor and his co-workers.

These studies began with the observation of Patek and Taylor[42] that from the blood plasma of normal human subjects there can be precipitated by dilution and acidification a globulin fraction that contains a clot-promoting substance for hemophilic blood. The material is active while fresh, or after drying in a vacuum. The same treatment of hemophilic blood yielded a precipitate that had little or no clot-promoting ability. Tested in a calcium-fibrinogen system, precipitates from both normal and hemophilic blood had equal prothrombin activity.

Later studies[43-45] demonstrated that both prothrombin and fibrinogen could be removed from this globulin substance without impairing the clot-promoting faculty for hemophilic blood. Further fractionation then demonstrated that all this clot-

promoting activity could be found in a euglobulin fraction. From these studies and from those of Howell,[40, 41] it becomes clear that the essential defect in hemophilia is the absence or deficiency of a euglobulin fraction of the plasma, which, in terms of the classic theory, may be designated as "plasma thromboplastin."

This observation immediately directs attention to the blood platelets. Quick[39] observes:

> Thromboplastin is widely distributed in the body as an intracellular substance. In the blood it occurs locked up in the platelets and perhaps is present also in the leukocytes. Certain tissues, notably the brain, lungs, and thymus, are particularly rich in thromboplastin. It apparently never occurs free, but is liberated whenever tissue cells are injured or ruptured. *In blood uncontaminated by tissue juices, the thromboplastin is liberated solely by the platelets. The liberation of thromboplastin by the platelets, therefore, appears to be the prime factor in determining the clotting time of blood obtained by venipuncture* [italics mine].

It is, of course, well known that no quantitative change in the platelets exists in hemophilia, and the reviews of the question of qualitative changes by Quick and Howell yield no very convincing evidence. It is equally recognized that great reduction in platelets may occur in thrombocytopenic purpura without change in the coagulation time of venipuncture blood. In view of these and other doubts cast on the platelet origin of plasma thromboplastin, Lozner and Taylor[46] have recently completed a most interesting study on the effect of foreign substance on blood coagulation.

The orientation of their work may be described most effectively by direct quotation:

> It has been known for many years that the coagulation time of blood taken in paraffin tubes is much longer than that of blood taken in glass tubes. The explanation usually afforded is that the glass, acting as a foreign surface, destroys the platelets at a more rapid rate than occurs in the presence of paraffin. The increased amount of thromboplastin so liberated is then considered to be responsible for the shorter coagulation time in glass vessels. Nolf has criticized this explanation. He states that his experimental data indicate that cell- and platelet-free plasma already contains all the factors necessary for blood coagulation. He believes that the initiation of coagulation is the result of direct modification of one or more of the constituents of cell-free plasma by contact with a foreign surface such as glass.

Four types of experiments were carried out, normal human blood obtained by clean venipuncture being used. In the first series, normal human plasma was employed without the addition of anticoagulants. The blood was drawn in an oiled syringe and transferred to a Lusteroid (a synthetic plastic) tube. Centrifugation at 4200 revolutions per minute for ten minutes gave a clear plasma with a platelet count of 8000 per cubic millimeter, essentially "platelet free." The plasma was then transferred to tubes of different materials in collodion pipettes, and the coagulation times determined. This was 11 minutes in glass, 64 minutes in collodion, 44 minutes in paraffin, and 49 minutes in Lusteroid. Since the plasma was platelet free, it must be concluded that all the elements necessary for coagulation were present in the plasma at the time it was removed from the centrifuge, and that the accelerating effect of glass was not exerted on the platelets.

In the second series of experiments, blood was transferred into Lusteroid tubes containing citrate, and a platelet-rich plasma obtained by slow centrifugation. Samples were transferred to the four tubes and stored for an hour. No destruction of platelets was found in any of the tubes as determined by platelet counts at the beginning and end of the storage period. Nevertheless, when samples of the plasma were recalcified in Lusteroid, the plasma stored in glass showed a coagulation time of six minutes, whereas the coagulation times of the other plasmas were prolonged. When cell-free plasma was stored as described above and then recalcified in Lusteroid, the glass-stored plasma clotted in eleven minutes, whereas that stored in paraffin, collodion or Lusteroid clotted in from eleven to thirty-nine minutes. These experiments indicate that glass storage does not destroy platelets, but does bring about a change in citrated plasma, either platelet rich or platelet free, that promotes coagulation when calcium is added.

A third series of experiments demonstrated that storage in glass increases the clot-promoting activity of either cell-free or cell-rich plasma when added to hemophilic blood. Finally, it was found that the preparation of the globulin substance (Howell's plasma thromboplastin) in glass vessels yielded a product of far greater clot-promoting properties than that prepared in paraffin or collodion vessels.

The authors conclude:

> The foregoing observations show that the effect of foreign surfaces on blood coagulation are [*sic*] essentially independent of the intact platelet. These studies indicate that the site of action of such surfaces is dependent upon a factor which is present in normal cell-free plasma, independent of prothrombin and fibrinogen associated with the euglobulin fraction of the protein and concerned with the clot-promoting activity of plasma for hemophilic blood [that is, plasma thromboplastin, according to Howell's nomenclature]. That this globulin substance might be derived from damaged platelets cannot be excluded by the present observations. However, it is present in cell-free plasma, and foreign surfaces have entirely similar effects on platelet-free and platelet-rich plasma. The data presented clearly indicate that the effect of foreign surfaces is not accompanied by an increased lysis of the platelets prior to clot formation as heretofore assumed.

Taylor and Lozner tentatively offer Gortner and Briggs's[47] suggestion that glass activates thromboplastin by virtue of its surface electrical charge.

This evidence that all the necessary factors for clot formation are found in normal circulating plasma raises new and interesting problems. It seems to afford an explanation for the presence in circulating rabbit plasma of a clot-promoting factor observed by Parfentjev[48] and demonstrated by Taylor et al.[49, 50] to be a true thrombin. It is possible that, in the rabbit at least, the reaction of prothrombin, calcium and plasma thromboplastin is a continuous one, and that small quantities of thrombin are constantly being formed. Why this thrombin does not react with fibrinogen to form fibrin remains a question, but its presence without clot formation indicates the presence of an anticoagulant. One should recall both the observation of Lozner, Joliffe and Taylor[51] of a patient with a hemorrhagic diathesis, with prolonged clotting time associated with a circulating anticoagulant, and Quick's[39] belief that heparin is normally present, in combination with albumin, in circulating blood, where it exerts an antithrombin effect.

Neuromuscular Transmission

The recent work of Nachmansohn et al.[52–58] has introduced a decidedly new point of view into a subject that at times seemed to have degenerated into a controversy between proponents of the so-called "electrical" and "chemical" theories of neuromuscular transmission. These studies have in great measure concerned the discharge of the electric organs of certain fish, — notably, the torpedo, the ray and the electric eel, — in which the electric organ is composed essentially of modified muscular end plates arranged in series, all other muscular elements having disappeared in the evolution of the structure. In these organs, discharge caused by stimulation of the appropriate motor nerve is accompanied by the liberation of acetylcholine. The injection of acetylcholine produces an electrical discharge, and the previous injection of eserine increases and prolongs the discharge produced by nerve stimulation or by acetylcholine. Nachmansohn and his associates have also demonstrated the presence of a high concentration of acetylcholine esterase in the electric organ, a concentration that varies directly with the intensity of the electrical discharge.

Considering these facts together with the observations that acetylcholine esterase is present in all nervous tissue and that it is concentrated at the surface of the tissue rather than in the axoplasm, the authors come to the following conclusions: acetylcholine participates in nerve transmission in all parts of the nervous system, and is not specifically limited to junctional tissues such as the synapse and the neuromuscular junction; and, in some fashion, the liberation of acetylcholine is responsible for the development of the electrical discharge that characterizes the physiologic activity of all nervous tissue and is recognized as a surface phenomenon.

In addition, these studies reveal the concentration at the surface of the axon of a high concentration of vitamin B_1, and suggest that this hormone is also implicated in the metabolism of acetylcholine. The hormone is essential for the metabolism of pyruvate, one stage of which yields acetate, and in the absence of vitamin B_1, the acetylation of choline to form acetylcholine is deficient. These observations therefore suggest that one of the essential biochemical lesions in the polyneuritis of vitamin B_1 deficiency is a diminished formation of acetylcholine and a consequent failure of nerve transmission.

A satisfactory schema of neuromuscular transmission can be constructed if, in addition to the above, the recent studies of Eccles and his coworkers[59–63] are considered. These investigators have for a number of years studied the electrical events occurring at the neuromuscular junction and have succeeded in recording potentials that appear to be derived from the motor end plate itself. They have shown that curarization diminishes the intensity of this potential, and that when the intensity decreases to less than 30 per cent of its normal value, failure of transmission occurs. End-plate potentials show a slow decay, which permits summation of two successive potentials. If their combined height reaches 30 per cent or more of normal height, an impulse is set up in the muscle. Eserine antagonizes the action of curare by increasing the height of the end-plate potential.

There is therefore justification for the following theory of neuromuscular transmission: the impulse arriving at the end-plate from the nerve liberates acetylcholine; the acetylcholine produces the end-plate potential; and the end-plate potential excites the muscle. There is no reason why a similar mechanism may not operate in transmission in the simple nerve fiber, with a repeated sequence of acetylcholine liberation, action current and excitation of adjacent tissue. The well-known effects of action currents in stimulating surrounding tissue can be recalled. Recent studies of the effect of axon on axon[64] and muscle on its motor fiber[65] deserve attention.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

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CASE 28291*

PRESENTATION OF CASE

An eleven-year-old schoolgirl was admitted to the hospital because of pain "like a hammer blow" in the left flank, lower abdomen and thigh.

She had been in good health until nine months before entry, when there was a gradual onset of

FIGURE 1.

attacks of sharp, stabbing pain, beginning in the left costovertebral angle and radiating both to the groin and anterolateral surface of the left thigh as far as the knee and to the left lower quadrant of the abdomen. These attacks were aggravated by straining, coughing, sneezing and other sudden motions. They usually appeared in the afternoon, occasionally at night, when the patient lay in bed, and lasted up to an hour. They tended to increase in severity and in frequency. Aspirin afforded slight relief. There was no history of significant trauma.

On examination the patient appeared well developed. The chest and abdomen were normal. There was right lumbar scoliosis, and some spinal rigidity, with tenderness to the left of the second lumbar vertebra. All reflexes were intact, and there were no sensory disturbances. Naffziger's[1] test caused pain to radiate around into the left lower quadrant and down the anterolateral aspect of the thigh to the knee.

The temperature, pulse and respirations were normal.

Examination of the blood showed a red-cell count of 4,420,000 with 13.2 gm. hemoglobin, and a white-cell count of 9800 with 60 per cent polymorphonuclears. The blood Hinton reaction was negative. The urine was normal. A lumbar puncture gave clear fluid under an initial pressure equivalent to 100 mm. of water. Bilateral jugular compression caused a rise in pressure to 250 mm. in thirty seconds, with a fall to 160 mm. in one minute after release; there were normal oscillations with the respiratory cycles. The total protein of the spinal fluid was 34 mg. per 100 cc., and the gold-sol curve was 0011100000.

A roentgenogram of the spine showed marked curvature of the lower dorsal and lumbar vertebras toward the right. The individual bones and joints appeared normal, except for a large, sharply defined defect in the pedicle of the second lumbar vertebra on the left (Fig. 1). The uninvolved anterior portion of the pedicle was increased in density.

On the seventh hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. MARIUS N. SMITH-PETERSEN: I do not know what a pain like a "hammer blow" refers to, or whether that was the onset of pain or not. If it were the onset of pain, it might be significant; if it were persistent pain of a throbbing character, it might also be important—this statement is not clear. The hammer-blow pain might have been caused by a fracture superimposed on underlying disease.

Later in the history, we have a statement to the effect that the onset of pain was gradual and that the pain was sharp and stabbing in character. From this statement we can conclude that the hammer-blow pain probably did not refer to a fracture superimposed on disease.

The distribution of pain was extensive: local pain in the left costovertebral angle, accompanied by radiation pain to the groin and to the anterolateral surface of the left thigh, as far as the

*The cases published in the July 16 issue of the *Journal* were incorrectly numbered "28301" and "28302," instead of "28291" and "28292." To keep the correct total, this and the following case have been given the numbers of those omitted.

knee; and radiation pain in the left lower quadrant of the abdomen. The radiation pain described is consistent with a lesion involving the twelfth dorsal and the first and second, possibly the third, lumbar vertebras. From the subjective pain, then, we can localize the lesion at the dorsolumbar junction.

"The attacks were aggravated by straining, coughing, sneezing and other sudden motions." This is worth noting since the pain arising from a lesion impinging on the spinal canal would be aggravated by straining, coughing and sneezing.

"They [the attacks] usually appeared in the afternoon, occasionally at night, when the patient lay in bed, and lasted up to an hour." Freedom from pain in the morning can be explained on the basis that the patient got up rested and carried herself better than she did later on in the day when she became tired. The lateral curvature could have been aggravated, and secondary strain thrown on the site of the lesion. The pain could not have been extremely severe or could not have increased very much, because the patient was not brought to the hospital for nine months after the onset.

"There was no history of significant trauma." We have no right to suspect the presence of a fracture unless it were superimposed on an underlying diseased condition.

"All reflexes were intact, and there were no sensory disturbances." These findings point away from a lesion involving the spinal canal.

Naffziger's test aggravated the pain radiating to the left lower quadrant and to the thigh. In my opinion, this reaction does not help us in making a differential diagnosis.

The blood picture, including the white-cell and differential counts, is against an infection, such as osteomyelitis.

A lumbar puncture was done. The dynamics were normal, but the total protein (34 mg. per 100 cc.) was high for a child of 11, pointing to possible irritation of the meninges.

X-ray films showed a sharply defined lesion in the pedicle of the second lumbar vertebra on the left. The uninvolved anterior portion of the pedicle showed an apparent increase in density. The appearance is consistent with a cyst and with xanthoma. Giant-cell tumor should be mentioned, but the patient is too young and I have never seen a giant-cell lesion in this location. Tuberculosis must also be mentioned, but I have never seen tuberculosis involving the pedicle. Hemangioma is my final alternative, but, again, I have never seen one in this region. Personally, I favor a diagnosis of cyst or of xanthoma.

Dr. Laurence L. Robbins: I think I have seen this case before, so that it is not quite fair for me to interpret the films. I should say that the important diagnostic point, so far as the radiologist is concerned, is the area of rarefaction with a rather sharp line of increased density around a portion of the margin. There is increased density in the pedicle, as described. I should not consider tuberculosis, and I do not believe that it is a hemangioma, because the usual appearance of hemangioma of the vertebra is more that of coarse striations.

Dr. Smith-Petersen: What would be your best guess?

Dr. Robbins: I know the diagnosis, having seen the films before.

Dr. Tracy B. Mallory: I think it is fair to say, however, that the X-ray Department did not suggest the correct diagnosis preoperatively.

Would anyone care to make any other suggestion?

Dr. Ernest M. Daland: How do you rule out Ewing's tumor?

Dr. Smith-Petersen: I cannot rule it out.

A Physician: Is the scoliosis presumably entirely secondary?

Dr. Smith-Petersen: I think so. One cannot depend on the parents' observation. Time and again, one observes extreme scoliosis, just discovered. In this case, I think it is fair to say that it came on in response to pain.

Dr. Channing C. Simmons: You have said that a giant-cell tumor is rarely seen at that age. I have been thinking it over, and I can think of 4 patients who were roughly under fourteen. If you were to ask me for the exact ages, I could not give them.

Dr. Smith-Petersen: I had a patient at the age of twelve who, according to the pathologists, had a giant-cell tumor; as time went on, the diagnosis was changed to cyst.

Dr. Fuller Albright: One sees giant-cell tumors in children with hyperparathyroidism.

Clinical Diagnosis

Extradural tumor, at level of second lumbar vertebra.

Dr. Smith-Petersen's Diagnosis

Cyst, involving pedicle of second lumbar vertebra.

Anatomical Diagnosis

Osteoid osteoma of second lumbar vertebra.

Pathological Discussion

Dr. Mallory: This patient was operated on by Dr. W. J. Mixter. The only preoperative diagnosis recorded is "tumor of the spine." They did

not commit themselves any closer. An evident tumor mass, consisting of obviously abnormal, rather soft bone, was found in the lamina of the second lumbar vertebra, and that, together with the transverse process, which was slightly involved, was removed. Microscopic examination showed a focus of intertwined osteoid trabeculae separated from each other by narrow bands of relatively acellular fibrous tissue. At the periphery of the lesion, the cortical bone was denser than normal. The picture is very characteristic of what Jaffe and Lichtenstein[2] have described as osteoid osteoma.

DR. SMITH-PETERSEN: As a matter of fact, Dr. C. B. Larson made that diagnosis. I talked this case over with him, and he suggested "osteoid osteoma."

DR. LARSON: It is unusual to find a punched-out lesion without more sclerosis of the bone around it.

DR. JACOB LERMAN: Did it involve the spinal canal?

DR. MALLORY: The operative note does not make that clear.

DR. SMITH-PETERSEN: It must have infringed on the spinal canal.

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CASE 28292

PRESENTATION OF CASE

First admission. A forty-nine-year-old white widowed painter was admitted complaining of inability to see to either side.

The patient was well until one year before admission, at which time he developed colicky pains in his abdomen, with nausea and vomiting in the morning. At the same time, he had gripping pains in both legs. There was also a feeling of weakness and lassitude. Some teeth were extracted, and a "lead line" of the gums was noted. Following this, he improved, although he continued to feel weak. Ten months before admission a physician examined his eyes; although the patient had no complaints, he was advised to wear glasses. The visual fields were normal. Three months prior to entry he noticed dimness in the left visual field of his left eye. This gradually increased. Three weeks before entry, it was thought that his left frontal sinus was at fault, and it was operated on. Immediately following the operation, the patient noted that he could not see well to the right side with his right eye. A few days after this, his nausea and vomiting recurred. He had had rare headaches, but these had not increased during the last two years.

The patient had been a painter for eighteen years. One brother had diabetes. Seventeen years before entry, the patient had been kicked on the forehead by a horse, and five stitches had been taken; he had had no residual symptoms.

Physical examination showed a well-developed and well-nourished man in no distress. All but two lower teeth were missing. There was a slight postnasal discharge. Examination of the chest was negative. The remainder of the general physical examination was negative. Neurologic examination showed normal mentality. The fundi were normal except for slightly dilated vessels. The visual fields showed bitemporal hemianopsia. External ocular movements were normal, and there was no nystagmus. The pupils reacted normally to light and accommodation. The remaining cranial nerves were negative. The reflexes were normal and equal on both sides. There were no other neurologic abnormalities.

The blood pressure was 155 systolic, 100 diastolic. The temperature was 97.4°F., the pulse 80, and the respirations 20.

The urine showed a specific gravity of 1.012 on one occasion and 1.008 on another, but was otherwise normal. The blood showed a red-cell count of 4,200,000 with 60 per cent hemoglobin, and a white-cell count of 6800 with 72 per cent polymorphonuclears. A lumbar puncture showed an initial pressure of 175 mm. of water, which rose to 350 mm. with jugular compression on either side and fell normally to 180 mm. After withdrawal of 10 cc. of fluid, the pressure was 120 mm. The fluid contained 1 lymphocyte per cubic millimeter and 49 mg. of protein and 70 mg. of sugar per 100 cc. The gold-sol curve was 0011100000. The spinal-fluid Wassermann reaction was negative. A blood Hinton reaction was negative.

X-ray films of the skull showed no evidence of increased intracranial pressure. The pineal body was not definitely calcified. The sella turcica was quite abnormal in size and shape: it was greatly enlarged; the posterior clinoid processes were displaced backward, and the one on the right showed evidence of erosion and decalcification; and the right floor of the sella showed evidence of erosion. There was increase in the size of the lower jaw, and all the bones of the skull appeared slightly thicker and denser than normal. The hands showed increased length of all the bones and slight tufting of the terminal phalanges. The bones of the feet were abnormally large.

A course of deep x-ray therapy was given over the pituitary gland: 800 r to the left sella, 800 r to

the right, and 600 r to both the anterior and posterior portions of the skull. After the third treatment, the patient was subjectively much improved and noticed a clearing of his visual fields. After his full course of therapy, however, visual-field determinations showed that there were still bilateral defects. On the thirty-first hospital day, an operation was performed. Between the optic nerves, which were definitely separated, was a bulging, blue-gray tumor, evidently arising in the pituitary fossa. It was explored with a needle, and about 5 cc. of brown fluid removed. The capsule was then incised, and a considerable amount of tumor curetted out. The sac seemed to be completely emptied but could not be removed because of the presence of large vessels. Pathological examination of this specimen revealed dense connective tissue containing large thin-walled vascular channels, but no epithelium. The patient improved rapidly following the operation and was discharged on the forty-ninth hospital day, with instructions to return after two weeks for visual-field examinations.

Second admission (six years later). The patient was not re-examined until one year after he was discharged, at which time visual fields showed moderate generalized narrowing on both sides. He had had no complaints until two years before his second admission, when he began to see dark spots in front of his eyes, associated with dyspnea, at the same time feeling as though he would drop. Six months before admission, he was unable to sleep well. Two months later, he had an attack of "flu," characterized by weakness, malaise and fever, and remained in bed for three weeks. Following this, he was weak and fatigued; his speech became slow, and anorexia severe. Intermittent nausea and vomiting recurred. There was no evidence of blood in the vomitus, and the vomiting was not projectile in type; it usually occurred immediately after a meal. The patient had had no headaches or convulsions. During the previous three months, he had noticed an increased sensibility to cold weather and generalized muscle aches. Two months before entry, visual-field determinations in the Eye Clinic showed marked narrowing on all sides, especially in the upper temporal fields. The visual acuity was 20/20 in the right eye, and 20/30 in the left. The fundi showed slight atrophy of the nasal side of each disk. Six weeks before admission, the patient entered the Thyroid Clinic, where a basal metabolic rate of –21 per cent was found. His skin was dry, and there was slight myxedema of the neck and face. A slowing of his mental processes was noted. Thyroid therapy was begun. During the previous two years, his weight had dropped from 210 to 175 pounds.

Physical examination on entry showed a slightly obese, well-developed and well-nourished man in no distress. The skin was pale and soft, but not dry or brittle. The hair was soft and silky, and the hair over the body was decreased in amount. The face was puffy. Examination of the fundi was essentially negative. The visual acuity was 20/20 in each eye. The visual fields showed only slight bitemporal narrowing, more marked on the right. The tongue deviated slightly to the right. Examination of the chest was negative. The abdomen was normal. There were no other pertinent findings.

The blood pressure was 140 systolic, 88 diastolic, lying down; 138 systolic, 92 diastolic, sitting; and 118 systolic, 92 diastolic, standing. The temperature was 98.6°F., the pulse 72, and the respirations 20.

Urine examination showed a specific gravity of 1.018; there were no abnormal findings. The blood showed a red-cell count of 4,100,000 with 65 per cent hemoglobin, and a white-cell count of 8000 with 41 per cent polymorphonuclears, 11 per cent large lymphocytes, 27 per cent small lymphocytes, 10 per cent mononuclears, 7 per cent eosinophils, 2 per cent basophils and 2 per cent unidentified cells. The smear showed slight achromia. The nonprotein nitrogen of the serum was 27 mg. per 100 cc., the chlorides 96 milliequiv. and the sodium 130 milliequiv. per liter, and the cholesterol 170 mg. per 100 cc. A sugar-tolerance test showed 87 mg. per 100 cc., fasting; 121 mg., in half an hour; 84 mg., in one hour; 98 mg., in two hours; and 112 mg., in three and a half hours. A blood Hinton reaction was negative. The basal metabolic rate was –22 per cent. A stool examination was guaiac negative. An electrocardiogram showed rather low voltage of the QRS complexes and T waves.

X-ray films of the skull showed marked enlargement of the sella, with marked decalcification of the dorsum sellae and posterior clinoid processes. There was no evidence of increased intracranial pressure. Films of the hands showed that all the bones were rather heavy; there was questionable tufting of the terminal phalanx of the fourth right finger. The chest films showed multiple areas of calcification scattered throughout both lung fields, particularly marked in both apical fields. The heart was normal.

The patient was given a high-salt diet and salt in gelatin capsules. Progressive improvement was obvious subjectively and objectively, and within twenty-four hours, his weakness and malaise had diminished considerably. He was discharged on the thirty-second hospital day.

Final admission (nine months later). The patient was seen one month after discharge, at which time his improvement had continued. A serum sodium at that time was 131 milliequiv. per liter, a potassium 3.8 milliequiv. and a total fixed base 139 milliequiv. Four months before re-entry, he developed general malaise, weakness, lassitude and aching in the joints. Following this, he had occasional fainting spells preceded by a feeling of increased weakness and perspiration. Many of these impending attacks were warded off by absolute rest and sugar by mouth. Two weeks before admission, on closing his right eye, he noticed that the temporal half of his left visual field was blind. He had no other complaints. He had gained 10 pounds in weight during the previous four months.

Physical examination showed a well-developed and well-nourished man in no distress. The skin was dry, pale, parchmentlike and cold. The hair of the scalp and pubic regions was rather scanty. There was no bulging about the craniotomy scar. Examination of the chest was negative. The abdomen was normal. The fingers were enlarged. The testicles were somewhat smaller than normal. Neurologic examination showed that the patient was intelligent and co-operative. His speech was slow. The pupils were equal and active. External ocular movements were full, without nystagmus. The fundi were normal. Visual-field determinations showed a left temporal hemianopsia and dimness in the right temporal field. Visual acuity was 20/20 in the right eye, and 20/50 in the left. The remaining cranial nerves were normal. Motor and sensory examinations were negative except for slight impairment of the vibratory sense over the left foot and ankle.

The blood pressure was 150 systolic, 105 diastolic. The temperature was 98.6°F., the pulse 70, and the respirations 20.

Examination of the urine was negative. The blood showed a red-cell count of 4,850,000 with 75 per cent hemoglobin, and a white-cell count of 6100 with 45 per cent polymorphonuclears, 50 per cent lymphocytes, 2 per cent mononuclears and 3 per cent eosinophils. A blood Hinton reaction was negative. The fasting blood cholesterol was 180 mg. per 100 cc. The serum sodium was 132 milliequiv. per liter, and the total fixed base 141 milliequiv. A lumbar puncture showed normal pressure and normal dynamics. The fluid was clear and contained only 2 lymphocytes per cubic millimeter. The total protein was 93 mg. per 100 cc., and the sugar 59 mg.; the gold-sol curve was 0001110000.

X-ray films of the chest showed no change since the previous examination. Those of the skull were essentially the same.

On the twentieth hospital day, an insulin-tolerance test was done following a dose of 6 units of insulin; the blood-sugar levels at twenty, thirty, forty-five, sixty, ninety and one hundred and twenty minutes were 81, 58, 62, 68, 83 and 93 mg. per 100 cc., respectively. The corresponding blood pressures were as follows: 150 systolic, 100 diastolic; 130 systolic, 90 diastolic; 104 systolic, 70 diastolic; 110 systolic, 76 diastolic; 120 systolic, 80 diastolic; 136 systolic, 30 diastolic; and 136 systolic, 98 diastolic. A course of x-ray therapy was given, which included 1200 r to each of four portals. Following this, the patient's condition was essentially unchanged. On the thirty-fifth hospital day an operation was performed.

Differential Diagnosis

Dr. Edward C. Reifenstein, Jr.: This is a very interesting case history. Let us retrace the involved course of events from the time that the patient became ill one year before his first admission to the hospital, which was about seven years before his second operation.

The first episode described in the history was an acute attack of abdominal colic, nausea, vomiting, gripping pains in the legs, weakness and lassitude. Such symptoms in a man who has been a painter for eighteen years and who is found to have a lead line of the gums indicate an acute attack of lead poisoning. The pains in the legs were probably manifestations of peripheral neuritis, which is not uncommonly seen in plumbism. It is interesting that the patient recovered from this neuritis without exhibiting a paralysis of the most used muscles of the legs, which is frequently encountered in acute intoxication with lead. It seems to me most unlikely that the lead poisoning had anything to do with the events that followed.

Nine months later the patient developed his next symptom: dimness in the left visual field of the left eye. The first thought that occurs to one is that the eye symptoms were related to the attack of lead poisoning and, hence, that the patient was developing an optic neuritis. The recurrence of nausea and vomiting shortly afterward also calls to mind the nausea and vomiting that were present during the attack of plumbism. However, nausea and vomiting do not usually present themselves as symptoms of plumbism in the absence of colic. Although it has been observed frequently that patients who have a considerable deposit of lead in their bones are apt to develop symptoms of acute intoxication with lead during a severe or protracted illness, in the present case, the patient, at the time of the recurrence of the nausea and vomiting, did not seem to have been sufficiently ill to have induced such a recurrence of

plumbism. Furthermore, the lack of other manifestations of lead poisoning and, particularly, peripheral neuritis at this time makes this interpretation doubtful. The demonstration of normal optic disks and bitemporal hemianopsia and the infrequency of the headaches help us to eliminate the question of lead intoxication from further consideration.

The finding of bitemporal hemianopsia immediately suggests an intracranial lesion, which provides a more likely explanation for the occurrence of nausea and vomiting. The slightly dilated retinal vessels, the slightly increased cerebrospinal-fluid pressure, the slightly increased cerebrospinal-fluid protein in the absence of cells, and the weak Type II gold-sol reaction are consistent with this interpretation. Furthermore, the bitemporal hemianopsia serves to localize the lesion as impinging on the optic chiasm. The x-ray evidence of a greatly enlarged sella turcica, with backward displacement of the posterior clinoid processes and erosion of the one on the right and the right floor of the sella, makes the picture complete. The clinical diagnosis of an intracranial lesion in the region of the pituitary gland warranted a trial of x-radiation therapy. When this proved ineffective, operation was indicated in an effort to protect the eyesight. The demonstration of the tumor mass at operation supplied the final proof of the correctness of the clinical diagnosis.

The major diagnostic problem in this case is the nature of the tumor mass that was found at operation. Before considering this, however, let us follow the subsequent course of the patient. For four years after the first operation, the patient was relatively free from symptoms. It is therefore reasonable to assume that the tumor mass, which seemed to be arising in the pituitary fossa, had not, up to that time, destroyed enough of the pituitary gland to interfere seriously with its function.

Two years before the second operation (four years after the first operation), however, a new sequence of events appeared. Not only did the visual symptoms become worse, suggesting that the tumor mass was again causing pressure on the optic chiasm, but, in addition, the patient developed increasing signs of insufficient function of the anterior pituitary gland. From a clinical point of view, the patient began to exhibit a considerable degree of so-called "panhypopituitarism" — that is, underfunction of all the elements of the anterior pituitary gland. There was evidence of inadequate function of the adrenal cortex: weakness, malaise and fatigue; Addisonian crises, with anorexia, nausea and vomiting; a loss of 35 pounds of weight; slight fall in blood pressure (from 155 systolic, 100 diastolic, on the first admission to 140 systolic, 88 diastolic); low serum sodium, chloride and total base values; and clinical improvement with a high-salt intake. There was also evidence of underfunction of the thyroid gland: increased sensibility to cold; dry, pale and soft skin; myxedema of the face and the neck; poor myocardial tone; generalized muscular aches; slowness of the mental processes; and a diminished metabolic rate. The fact that the basal metabolic rate on the second admission to the hospital was still –22 per cent in spite of thyroid therapy, which had been started six weeks before (and presumably was continued), suggests that the patient was not suffering from true myxedema (which would have responded by then), but rather from hypofunction of the thyroid gland secondary to underfunction of the anterior pituitary gland (which often fails to respond adequately to the usual thyroid therapy).[1] There was some evidence, furthermore, that the gonads were underfunctioning: a decrease in the amount of body hair; and testes somewhat smaller than normal. The glucose-tolerance test revealed increased tolerance: that is, the patient was hyperglycemia resistant. This finding is consistent with panhypopituitarism.[2] In spite of a high-salt intake and thyroid therapy, the patient began to have attacks of faintness associated with increased weakness and perspiration. These attacks were probably hypoglycemic attacks, since patients with panhypopituitarism are subject to such episodes, and since the attacks were controlled by the ingestion of sugar. There is no definite statement in the history that the patient was still receiving thyroid medication, but if so, this therapy may have induced the hypoglycemic attacks. We have seen several similar patients in whom this occurred. Thyroid medication also frequently induces Addisonian crises in these patients.

All these data make a strong case for the existence of a state of panhypopituitarism during this period. The one disturbing feature is the result of the insulin-tolerance test, which was normal. One would expect in panhypopituitarism to have hypoglycemia unresponsiveness — that is, inability to raise the blood-sugar level after an insulin-induced hypoglycemia. Furthermore, a full dose of insulin (0.1 unit per kilogram of ideal body weight) was given without any reaction, whereas patients with panhypopituitarism are so sensitive to an insulin-induced hypoglycemia that it is customary to give only a half to a third of the calculated dose of insulin to avoid reactions. In thus attaching significance to the insulin-tolerance test, we are assuming that the patient was properly prepared for the test by being placed on a diet containing at least 300 gm. of carbohydrate for at least three days prior to the test, and that he was

fasting for exactly twelve hours before the test was begun. If these conditions were not observed, the results of the test must be discarded.

It is unfortunate that we do not have available the results of 17-ketosteroid assays in this patient. This test measures the excretory products of the adrenal glands and the testes.[3] In panhypopituitarism, the levels are almost invariably less than 0.5 mg. of steroid per twenty-four hours — that is, for practical purposes, negative. If we accept as valid the results of the insulin-tolerance test, we must assume that some normal anterior-pituitary-gland tissue was still present and, therefore, that the 17-ketosteroids would not be negative, although they undoubtedly would be low, perhaps about 2 to 3 mg. per twenty-four hours.

The increase in visual disturbance with atrophy of the nasal side of each disk, along with the gradual onset of some degree of pituitary underfunction, indicates that the tumor mass was again causing pressure on the optic chiasm. This is substantiated by the definite increase in the spinal-fluid protein level. Since x-ray therapy was again ineffective, the only recourse was to attempt to remove the tumor surgically, in the hope of saving the eyesight.

Let us now consider what lesions may cause pressure on the optic chiasm. In order of frequency are found: an adenoma of the pituitary gland, a so-called "suprasellar cyst" or craniopharyngioma and, finally, a lesion such as a glioma of the chiasm, a meningioma arising from the floor of the third ventricle, a tumor such as a chordoma or a cholesteatoma, or even a chronic circumscribed arachnoiditis. The chiasm is also occasionally compressed from one or both sides by an aneurysm or varicose dilatation of one or both carotid arteries. However, since bitemporal hemianopsia was present in the case under discussion, and since this disturbance rarely occurs except with pituitary adenomas or suprasellar cysts, we can limit our discussion to these two types of lesions.

There are three types of anterior pituitary adenomas: the eosinophil (acidophil), the chromophobe and the basophil, corresponding to the three types of cells found in the gland. The basophil adenomas are extremely rare, and never attain an appreciable size; therefore, in view of the x-ray evidence of a large lesion and the findings at the first operation we can eliminate this type of adenoma from further consideration.

Eosinophil adenoma is a tumor of hormone-producing cells and it thus accompanied by evidence of increased production of these hormones. These hormones would produce acromegaly in a man of forty-nine. Are there any evidences of acromegaly in the patient under discussion? There is no history of an increase in the size of the jaw, head, hands or feet. In x-ray films of the jaw and skull, the bones were interpreted as thicker and denser than normal; also the bones of the hands and feet were stated to be increased in length or "abnormally large." But large or long bones do not necessarily mean acromegaly unless there is a history of a recent increase in the size of these bones. The increased density of the bones can be explained just as well as the result of the chronic deposition of small amounts of lead in the bones over a period of eighteen years. At one time, it was thought that tufting of the terminal phalanges was diagnostic of acromegaly; we have since found this manifestation in many other conditions and now attach no particular significance to it. One of the findings on x-ray study that is of great help in diagnosing acromegaly is an increase in the anterior dimensions of the bodies of vertebras, particularly the thoracic vertebras. This is seen best in lateral films taken over the thoracolumbar spine. Unfortunately this film was not taken. As a result of this change, the patient is not able to bend over and touch his feet. This disability is not mentioned in the physical examination of our patient, and therefore may be assumed to be absent.

Another test of considerable diagnostic aid in acromegaly also was not done: the level of the phosphorus in the blood serum. Since patients with acromegaly are growing, the phosphorus level is almost always significantly elevated (4 to 6 mg. per 100 cc.) compared with the normal adult levels (about 3 to 4 mg.).[4] In fact, the level in acromegaly approaches that of a growing child.

Although the finding of hyperglycemia resistance is characteristic of panhypopituitarism, it may occur in acromegaly during the stage of so-called "compensatory hyperinsulinism." As a matter of fact, there is considerable variation in the type of curves obtained in the glucose-tolerance, the glucose-and-insulin-tolerance and the insulin-tolerance tests in acromegaly, and the sugar curves are thus of no aid in the diagnosis of the condition.[2]

In view of the lack of history of an increase in size of the acral parts, and the absence of the x-ray films of the spine and of serum-phosphorus values, all of which are commonly employed as diagnostic tests by the endocrine consultants of the Massachusetts General Hospital, we must conclude that acromegaly was not seriously considered by the physicians in charge of this patient during his stay in the hospital. Since all the reported x-ray findings are capable of another interpretation than acromegaly, I believe that this patient did not have an eosinophil adenoma. Furthermore, eosinophil adenomas are said to be sensitive to x-radiation, and the lack of response in our patient to two different courses of radiation is additional evidence

against this diagnosis. However, in dismissing an eosinophil adenoma, it must be pointed out that chromophobe adenomas have been reported that have had a small number of eosinophil cells in them.

Final pathological diagnosis, therefore, rests between a chromophobe adenoma of the anterior pituitary gland and a craniopharyngioma. This is a very difficult decision clinically, since either of these lesions could produce a picture in every way comparable to that of the patient under discussion. Neither of these lesions is hormone producing, so far as we know. The differentiation between them is at times of more than academic interest, particularly in early lesions, since it is occasionally possible to remove completely the craniopharyngioma and, thus, to cure the patient. Usually, however, all the cyst cannot be removed, and the danger of recurrence then exists. Successful complete removal of a chromophobe adenoma is very rare, and even in cases in which the tumor was presumably completely removed, the danger of recurrence is always present. In the patient under discussion, complete removal of the lesion was not possible; hence the differentiation between the two lesions is only of academic interest. As is apparent from the preceding discussion, recurrence of the lesion is of no help in the differential diagnosis.

The age of the patient at the time of the appearance of the tumor symptoms favors the diagnosis of chromophobe adenoma, which occurs oftenest in the third to fifth decade, and rarely before fifteen years. Although craniopharyngiomas are congenital tumors and may occur at any age, more than half of them appear in childhood, and the rate of frequency is much diminished in persons older than twenty years. The history of trauma to the head suggests a suprasellar cyst; however, the fact that the tumor did not become active until sixteen years after the accident makes this relation rather dubious.

From a statistical point of view, a chromophobe adenoma is about three times more likely than a craniopharyngioma. Of 2023 cases of intracranial tumors compiled by Cushing,[5] pituitary adenomas comprise about 18 per cent and congenital tumors about 6 per cent.

The x-ray findings on the whole, favor a craniopharyngioma. A chromophobe adenoma of the pituitary gland typically causes great ballooning of the sella turcica, and only about a third of the cases exhibit erosion of the bony framework of the sella. Irregular erosion of the clinoid processes and the dorsum sellae is the usual finding in craniopharyngioma. In the patient in question, great enlargement of the sella was present, which favors a chromophobe tumor, but the erosion of the posterior clinoid processes and the floor of the sella is more consistent with a suprasellar cyst. Unfortunately, the original films have been destroyed, so that we have to depend on the original interpretations without visualizing the films ourselves. No mention is made of calcification in the tumor area; this occurs in about three fourths of the cases of suprasellar cysts. We have to assume that it was not present. Since it is stated that the pineal body was not definitely calcified, it is likely that calcification was looked for in the region of the tumor.

The visual-field defects are stated to be more regular with a chromophobe adenoma than they are with a suprasellar cyst. In this patient, the lesions were quite consistently the same — bitemporal hemianopsia — and, hence, are in favor of adenoma.

The pathological findings at the first operation contribute some data to the differential diagnosis. The presence of a cyst favors a craniopharyngioma but does not exclude a chromophobe adenoma. Although the former is usually cystic, it may be solid; on the other hand, degeneration of an adenoma or hemorrhage into it is not uncommon. The brown fluid obtained by aspiration of the cyst might have occurred with either lesion. It would be interesting to know if crystals of cholesterin were found in this fluid, as might be expected in either lesion since they are both of epithelial origin. The presence of dense connective tissue and of large thin-walled vascular channels without epithelium suggests the stroma of a chromophobe adenoma; however, no strands of cells are described. We can more easily interpret these findings as the tough capsule of a suprasellar cyst; however, the epithelial lining of the cyst was not found.

In summing up the evidence, I believe that the most likely guess regarding the nature of the lesion is craniopharyngioma. The sequence of events was presumably as follows: an episode of acute lead poisoning; one year later, a craniopharyngioma became active and expanded to exert pressure on the optic chiasm, anterior pituitary function being adequate; first operation, a large part but not all the craniopharyngioma being removed; an interval of four years without symptoms; the craniopharyngioma again increased in size sufficiently to cause pressure on the optic chiasm and also destruction of most of the pituitary gland; an interval of two years before the second operation, with repeated evidence of underfunction of the anterior pituitary gland (panhypopituitarism) accompanied by attacks of hypoglycemia; and second operation, a large craniopharyngioma tumor mass being found that pressed on the optic chiasm and had destroyed most, *but not all*, of the pituitary gland. Some

normal anterior pituitary tissue was still present in all probability to account for the normal insulin-tolerance test.

Clinical Diagnoses

Pituitary cyst.
Panhypopituitarism, with marked adrenal insufficiency.
Circulatory failure (terminal).

Dr. Reifenstein's Diagnoses

Craniopharyngioma, pressing on optic chiasm and having destroyed most of pituitary gland.
Panhypopituitarism.

Anatomical Diagnoses

Pituitary adenoma, chromophobic type.
Atrophy of thyroid gland, parathyroid glands and testes.
Thrombosis of central adrenal vein, bilateral.
Infarction of adrenal medulla, bilateral.
Partial infarction of adrenal cortex, bilateral.
Pulmonary congestion and edema.
Pulmonary tuberculosis, healed, apical, bilateral.

Pathological Discussion

Dr. Tracy B. Mallory: This patient was operated on most reluctantly in a final desperate effort to save his vision, after it was evident that radiation therapy was accomplishing nothing. A cystic tumor was once again visualized in the region of the pituitary gland, and the contents of the cyst were aspirated. It was not possible to remove the tumor itself. Following operation the patient, as had been feared, did not do well. He developed an extensive facial erysipelas. This was gradually brought under control with sulfonamide therapy, and he seemed to have rounded the corner. Then, suddenly, he collapsed, developed acute pulmonary edema and died within a few hours.

The autopsy proved that Dr. Reifenstein was correct in his analysis of the endocrine abnormality. The hypophysis had been extensively destroyed by tumor, but a small remnant of the anterior lobe could be recognized. There was atrophy of the thyroid gland, which weighed only 9 gm. and showed, on microscopic examination, extensive fibrosis and lymphocytic infiltration. The parathyroid glands showed marked fatty replacement of the parenchyma, and the testes were moderately atrophic. The adrenal glands provided a surprise. Both showed fresh thrombosis of the central vein, with extensive venous infarction involving the entire medulla and inner third to half of the cortex. It seems very probable in retrospect that this bilateral adrenal infarction correlates with the sudden terminal change in the patient's condition.

The tumor of the hypophysis turns out to be a chromophobe adenoma, with extensive central degeneration and secondary cyst formation, rather than a true primary cystic tumor, such as a cranial myringioma. In checking back over the clinical record, I find that two determinations of the 17-ketosteroids were done but for some reason were not reported until after the patient's death. The figures of 2.0 and 2.8 mg. per twenty-four hours were obtained, which are exactly in the range that Dr. Reifenstein predicted.

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NAVAL MEDICAL OFFICER PROCUREMENT

Perhaps, as intimated in a letter appearing elsewhere in this issue of the *Journal*, undue emphasis has been placed on the need for medical officers in the United States Army. The fact remains that the proportional need for physicians in the Navy is just as great.

The Office of Naval Officer Procurement is located at 150 Causeway Street, Boston, and those to whom this particular branch of the service appeals can be assured that commissions will be promptly granted to properly qualified physicians and that, ordinarily, calls to active duty will soon follow.

WILLIAM HENRY WELCH AND THE HEROIC AGE OF AMERICAN MEDICINE

Dr. William H. Welch led a life of so much activity that it would at first seem impossible to give even a running account of his many interests within the covers of a single volume. The skill of the Flexners,* however, has enabled them to present an excellent picture of one of the great figures in American medicine, a man who lived at a time when rapid evolution was taking place in medical thought. The authors have seen fit to describe this as "the heroic age of American medicine." One doubts if the term "heroic" is entirely satisfactory to describe a period such as that which Welch influenced.

That Welch should have been such a great figure in medicine is surprising in view of the fact that his early leanings were toward a career as a teacher of the classics. To be sure, his father, uncles, grandfather and great grandfather had all been country doctors in Connecticut. Medicine was indeed a tradition in the family, and the father naturally expected his gifted son to follow in his footsteps. Moreover, there was much in common between them, as one can judge by the delightful account of the country doctor given in this volume. Few pictures have been more exquisitely drawn than the description of the daily life of Welch's father, who was close to the people not only as their medical adviser but also as their true friend and counselor. The characteristic of doing so much work at night, moreover, was inherited by his more talented son.

Welch went to Yale, where he had a brilliant career both as a student and as a popular man. He was taken into Skull and Bones, the highest honor his fellow students could give him. Always interested in the classics, young Welch was tempted for years to teach school, but his father kept urging him to take a medical course and envisaged his son as his successor in country practice at Norfolk. Bending to his father's desire, Welch entered the College of Physicians and Surgeons in New

*Flexner, S., and Flexner, J. T. *William Henry Welch and the Heroic Age of American Medicine*. 539 pp. New York: The Viking Press, 1941.

York City in 1872. There, during his second year, he earned his first microscope for the best report on Seguin's lectures on nervous diseases. Because the lectures were held in the middle of Saturday afternoons, they were not well attended, but Welch considered them the best lectures in the curriculum and got his microscope, at that time something of a novelty. There were no laboratories for students in the medical school, and although a few professors used microscopes, it never occurred to them to pass their knowledge on to the undergraduates. Welch learned his first pathology from Delafield, but he soon found that if he wished to go beyond the simplest rudiments of histology, he must study abroad. After his graduation, in 1876, therefore, he took his first trip to Europe. He worked in the laboratories of Germany and France, being particularly impressed by the work of Cohnheim, who gave Welch his first chance to do experimental work. It was this work on edema that led to Welch's original paper on the subject, published in March, 1878, just after he returned to America.

Fired by an enthusiasm for laboratory investigation, he sought a post with Delafield in the College of Physicians and Surgeons. There was no space available, however, for Welch to set up a laboratory, and after a long series of negotiations, he finally obtained his desired room in Bellevue Hospital Medical College. He somehow acquired six antique microscopes and, by May, 1878, had six students working on pathologic specimens. Thus began scientific laboratory instruction for medical students in America, an accomplishment that will be regarded in the future as Welch's greatest contribution to medical advance in this country. Slowly, he increased his laboratory, and his fame extended beyond the borders of New York. Finally, the offer came to go to Baltimore, in connection with the founding of the Johns Hopkins Hospital and, subsequently, of the medical school. It was difficult for young Welch to leave New York, and his decision was certainly not made easier by the fact that his oldest and closest friend, Frederic S. Dennis, used every inducement to keep him there. At last, the rift came, and the friendship was broken off by Dennis, much to Welch's grief. He was deeply disillusioned by the break and never again in his fifty years of association with great men did he allow anyone, either man or woman, to get close enough to him to hurt him as Dennis had done.

After another brief visit to Europe, Welch went to Baltimore, where he began his work in the fall of 1885. He was installed in a commodious two-story building quite in contrast to the so-called "laboratory" that he had occupied in New York. There, in October, 1891, Welch did an autopsy in which he showed that the tissues were filled with bubbles of gas. His bacteriologic examination led to the discovery of a new micro-organism, now known as *Clostridium welchii*. In addition to his own research, he stimulated investigation in others, and his laboratory became the center of activities in both pathology and bacteriology. The Johns Hopkins Hospital was opened in 1889, and Welch soon began to report on various diseases as they appeared in the hospital population. There was still no medical school, and to Welch fell the long and difficult task of leading the campaign for funds to establish one.

Whatever he said carried great weight, and so important had his decisions become, not only at Johns Hopkins but indeed in all medical schools in this country, that it was not strange that Mr. John D. Rockefeller and those nearest to him turned to Welch for advice in the spending of a part of the great Rockefeller fortune. Welch's name was known to Rockefeller not only for his work at Johns Hopkins but also as the founder and editor of the *Journal of Experimental Medicine*, the first scientific publication of its kind in this country. It was Welch, therefore, who laid the plans for the Rockefeller Institute for Medical Research, and his advice was widely accepted in many other fields. So great had his influence become that when two men were discussing what they would do if they had a million dollars for medical education, one instantly replied, "I should

give it to Dr. Welch." No one else in medicine in this country has ever established such a wide reputation for sound advice regarding matters of the teaching of medicine.

From his work in New York for the Rockefeller interests, he naturally spread into even wider fields and became a medical adviser to the whole nation. Few new projects were developed during the period of Welch's greatness that did not reflect, often directly, his influence. Later, he took his part in World War I, made an expedition to Japan and China and, at the age of seventy-five, established the Institute for the History of Medicine at Johns Hopkins as the culminating event in his long life.

Except for his early and close association with Dennis, Welch never had an intimate friend, and there was always about him an air of greatness, with a line of demarcation over which no one dared step. He was tolerant, pleasant and thoughtful, but always in a somewhat detached manner. Many people wished to read beneath the surface of his mind, but that was never possible. He was, however, sensitive in that he quickly reflected his environment. One notes his change of attitude toward his German teachers and friends after he had come to know American and English medicine better. He was not usually shaken, and it is said that on only one occasion, when he stepped into the post-mortem room of a soldiers' camp during the height of the influenza epidemic, did he ever appear startled and at a loss for a word. In spite of all the honors that were showered on him, he maintained his extreme modesty to the end, always going out of the way to be kind toward a junior colleague or even to a beginning student of medicine. His erudition was profound, for he could discourse on hundreds of topics in a fluent manner. He loved, nevertheless, the simple things of life, and nothing pleased him more than to join the motley crowd on a hot Sunday afternoon at the beach on Coney Island or to ride on the roller coasters with young people, with whom he immediately became friendly. He could, indeed, talk with the great without losing his stature and converse with the lowly without embarrassment to them.

This story has been delightfully told by the Flexners. From the biography, a true picture of Welch emerges, skillfully depicted by expert hands. This is an outstanding biography of a great physician — a man not always easy to evalulate, but one whose influence in medicine will long be felt, since he was one of the greatest of four or five men who have served to make medicine in America what it is today.

MEDICAL EPONYM

Pott's Fracture

This type of fracture was described by Percivall Pott (1713–1788), F.R.S., in *Some Few General Remarks on Fractures and Dislocations* (London: 1768). A portion of the text follows:

> . . . when by leaping or jumping the fibula breaks in the weak part already mentioned, that is within two or three inches of its lower extremity . . . the inferior fractured end of the fibula falls inward toward the tibia, that extremity of the bone which forms the outer ancle, is turned somewhat outward and upward, and the tibia having lost its proper support, and not being of itself capable of steadily preserving its true perpendicular bearing, is forced off from the astragulus [*sic*] inwards, by which means the weak bursal, or common ligament of the joint is violently stretched, if not torn, and the strong ones, which fasten the tibia to the astragalus and os calcis, are always lacerated, thus producing at the same time a perfect fracture and a partial dislocation, to which is sometimes added a wound in the integuments, made by the bone at the inner ancle. . . .

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

Case History: Fatal anaphylactic shock resulting from pituitary extract

A forty-two-year-old primipara, whose past history was irrelevant, entered the hospital with pneumonia when about three months pregnant. The medical history states that she had had rheumatic fever and mitral stenosis, although the autopsy did not confirm the diagnosis. Eleven days after hospital entry, during her convalescence from pneumonia, the patient spontaneously miscarried; the placenta, however, did not come away. One ampule of pituitary extract was given for the purpose

of stimulating uterine contractions to aid in expulsion of the placenta; this was followed immediately by severe shock. There was no hemorrhage. At first, the patient appeared intensely red and felt weak and dizzy, and thirty minutes later, vomiting and sweating occurred, the lips became cyanotic, and she was pulseless. She remained in a state of collapse. A transfusion of 600 cc. of blood resulted in improvement for the next seventy-two hours, but death occurred at the end of this time, following delirium and a rapid rise in the pulse, respirations and temperature.

According to the death certificate, the cause of this fatality was "pulmonary embolism." Autopsy, however, revealed pulmonary congestion, retained placenta and recent thrombophlebitis of the right femoral vein but no evidence of a pulmonary embolus.

Comment. This is a very interesting case. Fortunately, an autopsy was performed. This death must have been due to circulatory shock following the administration of pituitary extract; no other conclusion can be drawn. As stated above, the placenta was still in the uterus at the time of death.

These are not the times in which to try to revolutionize medicine, but it does seem as if there should be some means whereby cases that are autopsied may have the true anatomic diagnosis recorded on the death certificate. Too often, the pathologist's diagnosis does not coincide with that of the physician, and so long as this obtains, our vital statistics will be inaccurate.

DEATH

HARRIS — A. E. Harris, M.D., of Lynn, died July 11. He was in his seventy-third year.

Born in Montville, Maine, Dr. Harris received his degree from Bowdoin Medical School in 1895. He was a former member of the staff of the Lynn Hospital and a member of the Massachusetts Medical Society and the American Medical Association.

His widow and a brother survive him.

MASSACHUSETTS MEDICAL SERVICE

First Contract Initial Step in Complete Service

The public is not yet willing to buy complete medical-service contracts, according to the studies made by the Massachusetts Medical Society of the medical plans in operation in other states. Therefore, the Massachusetts Medical Service is initiating its program with a partial-coverage contract, which includes hospital surgery, obstetrics and diagnostic x-ray service.

This first contract is the initial step in evolving a complete medical-care service. Present plans indicate that the second contract will cover all hospitalized illnesses and that the third contract will cover hospital, office and home care so far as experience proves it advisable.

This gradual approach parallels the method used in developing the Blue Cross nonprofit plan for hospital care and is based on the necessity for educating the public gradually to the need for increasing expenditure to obtain more complete services. The Blue Cross contract was sold first to the individual subscriber on the basis of three cents per day; next, the subscriber was willing to spend more to protect both himself and his wife; and finally, the subscriber learned the value of buying a more expensive contract that would protect all members of his family under eighteen years of age.

Other States Point the Way

The wisdom of a gradual development of the Massachusetts plan is borne out by the experience of medical-service plans in other states, where complete coverage has met with poor public response.

In Michigan, 187,000 surgical-obstetric contracts were sold as against only 5816 contracts providing complete medical coverage. In one year alone, Michigan lost $75,000 on complete-coverage contracts, of which $10,000 was lost on a single employee group. California has sold only 30,000 complete-coverage contracts in six years, and only 10,000 have been sold in New York.

Premature Contracts Unsatisfactory

The premature sale of complete-coverage contracts to a public uneducated to them brings disastrous results in many instances. In some states, compensation to family physicians dropped to from twenty to sixty cents on the dollar. In other states, the medical-service corporation went into debt to maintain payments to physicians.

Buffalo, California and Michigan are selling no more complete-coverage contracts, and all the states that began with complete-coverage contracts have been forced to revert to the issuance of the surgical-obstetric contract. "The surgical-benefit contract is more or less predictable from an actuarial basis," writes Philo Nelson, general manager of the California plan, "and is the soundest to begin with." John Mannix, executive director of the Michigan Hospital Service, who is closely affiliated with the Michigan Medical Service, states, "From the experience of Michigan, partial coverage is the only approach that is reasonable." The wisdom of the partial-coverage contract is further confirmed in a preliminary report made by the Superintendent of Insurance of the State of New York, who says: "A greater appeal seems to exist for surgical benefits only than for general medical coverage. This is due, perhaps, to the possibility of being con-

fronted with much more substantial bills for surgical services than for general medical expense. It is understood that the plans contemplate experimenting to a greater extent in this field."

By enthusiastically and actively supporting the program of the Massachusetts Medical Service, physicians of the State may help to avert the appearance, in Massachusetts, of a bill similar to the following, which will be supported next year by the New York Insurance Commission unless the medical profession of that state takes active steps:

"A hospital corporation may, by amendment of its charter, acquire the power to supplement its contracts for hospital service by provision for the furnishing of indemnity against physicians' fees for surgical and obstetrical care rendered" (Hampton Bill, New York Senate No. 1273 In. 1054).

WAR ACTIVITIES

OFFICE OF CIVILIAN DEFENSE

How to Protect Yourself Against Gas

Two recent operations letters dealt with the establishment of improvised decontamination stations and with the organization of decontamination services, respectively. This letter deals with personal protection against gas.

The following information on war gases is supplied by the United States Office of Civilian Defense for general publication because of the possibility that such gases may, at some time, be used by the enemy. If people will remember a few simple facts, they will have no unreasonable fear of this agent.

* * *

War gases stay close to the ground, for they are heavier than air. To get out of a gassed area, simply walk against the wind or go upstairs.

Gas is irritating and annoying to the eyes, nose, lungs and skin, but it is usually harmless if you do not become panicky but promptly leave the gas area and cleanse yourself. A soldier must put on a mask where it is necessary to remain in the contaminated area, but a civilian can go up on the second or third floor and literally ignore it, if the windows are kept closed.

If the gas should get on your skin, you can prevent it from doing much harm by sponging it off as quickly as possible with a piece of cloth, such as a handkerchief, and applying some neutralizing substance, followed by a thorough bath, preferably a shower, with common laundry soap and water.

If you are indoors, stay there with doors and windows closed, and go up to the second or third story. Stay out of basements. Turn off air-conditioning equipment, and stop up fireplaces and any other large openings.

Some gases are spread as oily droplets, which blister and burn the skin and eyes. If you are outside when gas is used do not look up. Tear off a piece of clothing or use a handkerchief to blot any drops of liquid from your skin and throw the contaminated cloth away. Blot; do not rub, as rubbing will spread the liquid. Then go home, if it is nearby, or to the nearest place where you can wash immediately with soap and water and cleanse yourself in the following manner:

(1) Remove all outer clothing outside the house, since gas can be transmitted to others from contaminated clothing. Put it preferably in a covered garbage pail.

(2) Apply one of the following effective household remedies to the part of your skin that has been contaminated: Chlorox or a similar household bleach (for mustard gas); peroxide of hydrogen (for Lewisite); a paste or a 2 per cent solution of baking soda (one tablespoonful to a quart of water), if you have no bleach or peroxide. If you do not know the gas, use both bleach and peroxide. Keep the bleach and the peroxide out of the eyes. *Do not waste time looking for these remedies*: bathe *immediately* if they are not at hand.

(3) After entering the house, wash the bleach or peroxide from the hands with laundry soap and water and then wash the face. Remove the underclothing, place it in a covered garbage pail and enter the bathroom.

(4) Irrigate the eyes with large amounts of a lukewarm 2 per cent solution of baking soda (one tablespoonful to a quart of water), or else with plain water. Use an ordinary douche bag or an eye irrigator. If you do not have these, let plain warm water pour into the eyes from the shower, washing them thoroughly. Do not press or rub the eyes.

(5) Lastly, take a shower, using laundry soap and hot water.

(6) If the nose and throat feel irritated, wash them out with the baking soda solution.

(7) If the chest feels heavy and oppressed, if you have any trouble breathing or if cigarette smoke becomes distasteful, lie down and stay perfectly still until a physician sees you.

(8) If blisters develop, be careful not to break them and call a physician.

Remember:

Soldiers require gas masks because they must remain in the contaminated area. Civilians can get out of the gassed area or get above the level of the gas, where they do not need gas masks or protective clothing.

Injured persons who are gassed require decontamination before they can be admitted to hospitals. All other civilians can best prevent any serious injury by promptly helping themselves in the manner outlined, using a kitchen or bathroom, laundry soap and water, and a few materials found in every household.

CORRESPONDENCE

NAVAL MEDICAL OFFICER PROCUREMENT

To the Editor: The imminent conscription of all medical skills for the war effort has been amply outlined and urgently stressed in your columns, especially in the issue of July 2. There has been a tendency among physicians to interpret this need and opportunity as one of service in the Army. Indeed, rumors have come to my attention that doctors were no longer needed in the Navy and that commissions in the Naval Reserve were not being granted or, if granted, the call to active duty was likely to be deferred.

All of us recognize the larger numerical need of the Army, but the proportional need of the Navy remains just as great. Current directives inform us that quotas of medical officers of the Naval Reserve have been greatly extended and that many more applications for commis-

sions should be obtained as promptly as possible. Furthermore, physicians commissioned in the Naval Reserve may ordinarily anticipate prompt call to active duty.

The Office of Naval Officer Procurement is located on the sixth floor of the North Station Office Building, 150 Causeway Street, Boston. Captain C. H. J. Keppler is in charge, and the office is open daily from 8:00 a.m. to 4:30 p.m. to receive applications or to supply information. If seriously interested local medical societies, hospital staffs or other medical groups at a distance from Boston desire a representative of the Naval Reserve Medical Corps as a speaker, every effort will be made to accommodate them.

LIEUT. COMDR. ROBERT S. PALMER, MC-V(S),USNR
Office of Naval Officer Procurement
150 Causeway Street
Boston

"REFUGEE PHYSICIANS"

To the Editor: We, the undersigned, as physicians who have come here from foreign countries in recent years, take note of the letter from Dr. P. C. Zanfagna, president of the Greater Lawrence Medical Association, published in the June 18 issue of the *Journal*.

The whole tenor of this letter is reminiscent of familiar propaganda attacking groups that are weakest from an economic and legal point of view, groups to which we, as immigrant physicians, belong.

Dr. Zanfagna refers to Massachusetts as a " 'dumping ground' for physicians not wanted elsewhere." In the course of recent immigration, approximately 200 immigrant physicians obtained licenses in Massachusetts. Not more, however, than 100 are in general practice, and they represent 1.26 per cent out of the total number (7889) of registered physicians. In 1942, immigration stopped.

The Board of Registration in Massachusetts is accused in this letter of licensing aliens "whose class of school and educational background cannot be verified." This is not true, since practically all these immigrant physicians graduated before 1933, when the status of their schools was known and had been verified by the American Medical Association and National Board of Medical Examiners. The same scientific and ethical qualifications were demanded of them when they took their state-board examinations in Massachusetts as are required of native physicians. When it is realized that the great majority of these physicians, who are between forty and sixty years of age, successfully passed the examinations despite the mental disaster they had experienced and the language hurdle they had to overcome, the allegation that they are "ignorant and incompetent" is nothing less than absurd. Most of these men had been in practice for fifteen to twenty years before they came to this country. The implication that spies or saboteurs can be guarded against by requiring citizenship as a condition of licensure strikes us as bordering on the preposterous.

The immigrant physician is not a little confused by the fact that, while the shortage of physicians mounts steadily, he, willing to serve in any capacity and not wanting to impose on native physicians or compete with them, stands waiting. Let him be taken into the Indian Service, or into a medically unmanned area in any state. He will go gladly if given the opportunity.

We agree that immigrant physicians should do military service along with native physicians; to state, however, that "Major Seeley does not want these men to treat our boys" is untrue. A number of the undersigned and others went to the Army Base on the very first day of the war to offer their services in any capacity; they were informed that the law prohibits the commissioning of noncitizen physicians. Practically all immigrant physicians responded to the request of the Procurement and Assignment Service and offered their services. The undersigned physicians, speaking on behalf of the majority of immigrant physicians in Massachusetts, take this opportunity to appeal to the Massachusetts Medical Society and the American Medical Association for help in becoming acceptable for military service, and whenever and wherever they may be needed. This is the least they can do to show their gratitude to this country, which gave them a haven of refuge and a new home.

Perhaps, those whose ancestors came to these shores as aliens should look back to those times and compare for themselves the former hospitality with what is extended to us by some of them today.

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Boston

REPORTS OF MEETINGS

MASSACHUSETTS TUBERCULOSIS LEAGUE

On April 9, the Diabetes Committee of the Massachusetts Tuberculosis League met at the Myles Standish Hotel, Boston. Under the leadership of Dr. Elliott P. Joslin, this committee has worked steadily against diabetes since its founding in March, 1935. The committee is very small, and its annually invited representatives are among those persons most interested in diabetes in the eleven largest hospitals of Boston.

Since the majority of deaths from diabetes occur in these hospitals, it was believed that the physicians concerned should be the ones to study most intensively prevention and treatment seeking to correct their own mistakes than to initiate, as was done in some other cities, a popular organization to combat diabetes. Various procedures have developed in combating diabetes as a result of repeated interchange of experiences on every phase of the treatment in the hospitals of Boston. Successive yearly meetings have recorded improved results.

Through the years, the physicians representing the hospitals have attempted to meet and discuss diabetes with physicians whose cases sent to the hospital have proved serious or obscure.

To the members of this committee come interesting bits of literature on diabetes. At the meeting was presented Volume I of the *Proceedings of the American Diabetes Association*, the first annual meeting having been held at Cleveland on June 1, 1941. Also presented was the first copy of *Diabetes Abstracts*, issued in January, 1942, a quarterly of the new American Diabetes Association. These abstracts, said by the physicians to cover the field splendidly, are produced at the expense of the Eli Lilly Research laboratories, which were already equipped to gather this material.

The Diabetes Committee consists of Dr. Elliott P. Joslin, chairman, Dr. Herbert Lombard, Dr. Alton S. Pope, Dr. Francis P. Denny, Dr. Charles F. Wilinsky, Arthur J. Strawson, secretary, and Dr. Henry D. Chadwick, ex-officio.

PLYMOUTH DISTRICT MEDICAL SOCIETY

The annual meeting of the Plymouth District Medical Society was held at the Bridgewater State Farm on April 16, 1942. The minutes of the previous meeting were read by Dr. R. C. McLeod.

Dr. R. A. Kruger reported small progress in the investigation of the group health insurance for the members of the society. At least one company would require 50 per cent of the membership to join. All policies would be on an annual basis and cancellable at the discretion of the company at the end of one year. It was Dr. Kruger's opinion that none of the companies were really anxious for this type of business. It was voted to poll the entire membership as to its wish to investigate the matter further. Dr. J. J. McNamara offered to present an insurance man at a later meeting to explain further.

The officers for the ensuing year were elected as follows: president — C. D. McCann; vice-president — E. L. Perry; secretary — R. C. McLeod; treasurer — A. L. Hurlburt; councilors — W. H. Pulsifer (nominating), P. H. Leavitt (alternate, nominating), J. E. Brady, W. T. Hanson, Charles Hammond, P. B. Kelly, G. A. Moore and D. W. Pope; censors — W. T. Hanson (supervising), J. H. Dunn, G. A. Buckley, H. F. Pierce and A. W. Carr; orator — W. C. Gould; librarian — J. H. Weller; and commissioner of trials — J. A. Carriuolo.

Dr. G. A. Moore, the retiring president, thanked the faithful members for their attendance and help throughout the year, and presented small tokens to the members present. Dr. P. H. Leavitt gave a report on progress in the Society's medical-insurance program. Dr. Moore presented Dr. F. E. Wheatley as orator. Dr. Wheatley also was orator twenty-five years ago and remarked that following both appointments a world war had occurred.

Dr. Wheatley's paper concerned roentgen-ray therapy. As early as 1904 in Boston, Dr. Francis Williams wrote a book on x-ray treatment, but early doses were uncontrollable. In 1914, the Coolidge tube, which allowed dosage regulation, was introduced. It was found that high-voltage machines give off as many nonpenetrating rays as low-voltage ones, and require screening with aluminum or other metals. In the early 1920's, potentials as high as 200 kilovolts were available. Huge doses under high voltage were thought lethal to new growths, but soon proved lethal to healthy tissues also. Repeated divided doses afford a better chance for the normal tissues to recover. Radiation for deep therapy is still in a chaotic state, since high-voltage treatment has been a disappointment. In inflammatory processes of acute nature, many small x-ray doses do very well. Precancerous lesions are best treated by small doses. A slowly growing lesion often requires heavier total dosage than the rapidly growing type. Advanced and hopeless cases of deep cancer can only be damaged, and such sequelae as burns and x-ray sickness may be worse than the disease itself, and may help to kill the patient sooner. The pros and cons of x-ray exposure before or after breast amputation are still under discussion. Some believe that perhaps 10 per cent more patients live five years after having x-ray treatment. In other constitutional conditions, such as leukemia, Hodgkin's disease and splenomegaly, rapid and massive dosage is a poor choice. Weaker doses have accomplished much more, and no fatalities have resulted for two or three years after treatment. The previous conception of x-ray therapy has been correlative to the idea of a cure of malignant tumors. In the speaker's opinion, more attention should be given to the palliative effects.

EDWARD L. PERRY, M.D., *Reporter*

BOOK REVIEWS

Shock Treatment in Psychiatry: A manual. By Lucie Jessner, M.D., Ph.D., and V. Gerard Ryan, M.D. With an introduction by Harry C. Solomon, M.D. 8°, cloth, 149 pp. New York: Grune and Stratton, Incorporated, 1941. $3.50.

A new kind of treatment for psychiatric disorders has been developed since 1928, when Sakel first began giving insulin in doses sufficient to produce hypoglycemic states. Insulin therapy was subsequently augmented, although not entirely replaced, by the Metrazol convulsive treatment of von Meduna, in 1933. The third method, — electric convulsive therapy, — introduced by Cerletti and Bini in 1937, is now extensively used, and in many clinics has displaced the more dangerous, less well-controlled shock treatment by insulin or Metrazol.

This small but excellent book covers the historical data, the details of the use of the three methods and their dangers, the selection of patients, the theoretical considerations and the effect of shock treatment on the course of various mental diseases. The manual is timely, accurate, sufficiently detailed and soundly written. There is a voluminous but selected bibliography. The price charged for a book of less than one hundred and fifty pages is quite high.

Body Mechanics in Health and Disease. By Joel E. Goldthwait, M.D., LL.D., Lloyd T. Brown, M.D., Loring T. Swaim, M.D., and John G. Kuhns, M.D. With a chapter, "The Heart and Circulation as Related to Body Mechanics," by William J. Kerr, M.D. Third edition, completely revised and reset. 8°, cloth, 316 pp., with 121 illustrations. Philadelphia: J. B. Lippincott Company, 1941. $5.00.

The main theme of this work is the effect of poor body mechanics on the various systems of the body. It is easy for one to appreciate the influence of improper posture on the joints and their supporting structures. Just as important, but far less obvious, are the secondary effects on digestion, circulation and respiration. The authors discuss the diagnostic features of poor body mechanics and outline the proper treatment for the various types.

This book deals largely with end results and, by emphasizing the evils, points the way to prophylactic care in early life, when habits are formed. A good bibliography is appended for more detailed study of the particular problems.

Edith Cavell. By Helen Judson. 8°, cloth, 288 pp. New York: The Macmillan Company, 1941. $2.50.

Edith Cavell's tragic story has often been told, but nowhere better than in this work by an author who has made a profound study of Miss Cavell's whole career. The book is well written and brings out clearly Miss Cavell's character, the type of work that she was engaged in as a nurse, the reasons for her being apprehended by the Germans and the details of her execution. Although much of this material has been known for years, Miss Judson has added new details of historical importance. The author, moreover, has been careful not to emphasize the emotional effect of Miss Cavell's death; she has written a straightforward account such as, one presumes, Miss Cavell would have approved herself. There is no hatred or bitterness in the book, and the standard followed is similar to that set by Miss Cavell in her famous remark: "I know that patriotism is not enough; I must have no hatred and no bitterness toward anyone."

(Notices on page ix)